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VOLUME 27
1932

PUBLISHERS
AMERICAN MEDICAL ASSOCIATION
CHICAGO, ILL.

Medical
Wain

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Archives of Neurology and Psychiatry

VOLUME 27 JANUARY, 1932 NUMBER 1

PROGRESSIVE PALLIDAL DEGENERATION

A NEW CLINICOPATHOLOGIC SYNDROME *

N. W. WINKELMAN, M.D.

PHILADEPHIA

At the meeting of the Philadelphia Neurological Society in December, 1924, Dr. F. X. Dercum [1] presented two brothers, each showing retinitis pigmentosa; the older had in addition a well marked extrapyramidal rigidity, and the younger had this condition in its incipiency. Dr. Dercum thought that the symptom group (the association of retinitis pigmentosa with rigidity) had not been described before. Since that presentation, the condition in both patients has progressed. The elder brother died in November, 1927, after an intense degree of rigidity had developed. The younger is still living. The brain and spinal cord of the elder brother were sent to my laboratory, where an intensive study was made. The history of the cases was supplied by Dr. Dercum.

CLINICAL REPORT OF CASES

CASE 1.—W. D., the elder brother, was a white man, aged 24, at the time of death. His chief complaints were dimness of vision and generalized rigidity. The family history was without significance, except for a late-appearing epilepsy in the mother. The weight was 10 pounds (4,535.92 Gm.) at birth. There were no abnormalities at the time of birth, and as a baby the patient was considered healthy. There were no childhood diseases, except mumps. At the age of 3 or 4 years, difficulty with vision was first complained of, in the form of night blindness. At the age of 11 years, atrophic changes were noted in the eyegrounds by Dr. L. Webster Fox. At 12, vision was so bad that he was sent to a school for the blind. At the age of 14, stiffness of the lower limbs began to be noticed; it soon interfered with walking. So rapidly did this stiffness progress that at the age of 16 he was compelled to leave school, and at 18 he was "helpless." Since the age of 18, the condition had advanced more slowly, and when the patient was presented by Dr. Dercum, in 1924, there was marked rigidity of both the upper and the lower extremities, and walking was impossible. The facial expression was fixed. The patient spoke slowly and enunciated with great difficulty and indistinctly. The

* Submitted for publication, Dec. 15, 1930.

* Presidential address read at a meeting of the Philadelphia Neurological Society, January, 1929.

* From the Graduate School of Medicine, University of Pennsylvania, the Laboratory of Neuropathology of the Philadelphia General Hospital and Temple University.

1. Dercum, F. X.: Two Cases of Retinitis Pigmentosa Occurring in Brothers, One Associated with a Spastic Symptom Group, Arch. Neurol. & Psychiat. **13**:651 (May) 1925.

knee and achilles reflexes were elicited, but were inhibited owing to the marked rigidity. Clonus and the Babinski sign were absent in both lower limbs. The reflexes of the upper limbs were exaggerated. The sphincters were under control. Sensation was intact. Hearing was not impaired. Physical exertion or emotion increased the rigidity. The blood pressure was 125 systolic and 85 diastolic. Laboratory examinations showed normal blood and spinal fluid. A roentgenogram of the skull revealed a rather small sella turcica. A special examination of the eyes by Dr. Hansell showed all the concomitants of retinitis pigmentosa: moderate horizontal nystagmus, clear mediums, atrophic optic nerves and peripheral pigmentation.

When W. D. came to the Philadelphia General Hospital he was in extremis and lived only one day, the clinical picture being confused by a terminal thrombosis of the superior longitudinal sinus. There was, however, such extreme rigidity and contracture that voluntary movement was barely possible.

Summary.—The clinical picture consists of retinitis pigmentosa beginning at the age of 3 or 4 years, with rigidity of the extrapyramidal type beginning at 12. It is of interest to note the complete absence of all forms of involuntary movements: tremor, chorea and athetosis. Blindness became complete at the age of 12. Rigidity was so intense that contractures resulted, and at the time of death voluntary movements were impossible. No pyramidal tract signs were present.

Case 2.—The condition of the brother, E. D., aged 19, began with dimness of vision and a complaint of night blindness. He had had to wear glasses since the age of 10 years. Speech had become slightly indistinct. Physically, he presented no abnormalities. Neurologically, he showed a slight rigidity of the entire body, with a set facial expression. The reflexes were increased, and there was an abortive ankle clonus. Sensation was normal. Examination of the eyegrounds showed that the media were clear; the disks were waxy in color, with the edges moderately blurred; the arteries were attenuated as they approached the disks; spots of pigment were scattered throughout the periphery of the fundus. A roentgenogram showed a small sella turcica in comparison to the size of the head. Laboratory studies revealed: spinal fluid, 4 cells; globulin, not increased; and the sugar content normal; the Wassermann test was negative. The blood count showed 4,920,000 red cells, 7,000 white cells and hemoglobin 90 per cent; the differential count was well within normal limits, and the Wassermann test of the blood was negative.

Comment.—The condition in these cases is familial. It is well known that retinitis pigmentosa may be familial or hereditary, and that it is often associated with other defects of development, in particular with defects in the nervous system. Because of the extrapyramidal symptoms in both these boys, attention was naturally directed to other hereditary or familial conditions of the basal ganglia, and it is to these that the major part of this work is directed.

To the group of familial or hereditary diseases affecting principally the basal ganglia belong: (1) Huntington's chorea, in which there is not only a degeneration of the cortex, which accounts for the mental symptoms, but a parenchymatous degeneration of both putamen and

caudate, or what has been called by the Vogts "striatum," in contrast to the globus pallidus or "pallidum." (In this presentation the terms striatum and pallidum will be used in this manner.)

(2) The Wilson pseudosclerosis group, or hepatolenticular degeneration, according to Hall, is familial and dependent on an inborn defect of the liver and brain in which exogenous causes play at most a precipitating rôle. The clinical syndrome described by Wilson [2] consists of generalized tremor, dysarthria and dysphagia, muscular rigidity and hypertonicity, emaciation, spasmodic contractions, contractures and emotionalism, associated with cirrhosis of the liver. The mental symptoms may be slight and are sometimes absent. Pathologically, there is usually gross damage to the lenticular nuclei, and in particular to the putamen, associated with cirrhosis of the liver. Sporadic cases occurring in families have been reported, giving Hall a basis for his statement that hepatolenticular degeneration may be familial. Barnes and Hurst [3] reported four cases in one family of a condition that Wilson [4] admitted "was quite consonant with that of progressive lenticular degeneration," although he apparently does not believe that progressive lenticular degeneration is familial.

(3) In 1922-1923, Hallervorden and Spatz [5] described a familial disease of the extrapyramidal system with involvement particularly of the pallidum and the pars reticularis of the substantia nigra. This condition, in brief, began in earliest childhood and was characterized by mental deterioration and increased tonus to the point of the production of contractures. In one sister there were also choreo-athetoid movements. In this family the disease developed in five of nine living children. At autopsy, the brain showed a brownish staining of the pallidum and the zona reticularis of the substantia nigra. Microscopically, the changes were most marked in the pallidum and the reticular part of the substantia nigra, but were present to a less degree throughout the entire brain. The pallidum and reticular part of the substantia nigra showed a marked increase of iron pigment and of large glia cells, but not those of the Alzheimer type, while the ganglion cells themselves showed no marked degeneration. Both centers were filled with a peculiar pigment that gave no true calcium reaction but contained iron. This pigment was contained not only in the glia cells and in the tissue

2. Wilson, S. A. K.: Progressive Lenticular Degeneration, Brain **34**:295, 1911-1912.

3. Barnes, S., and Hurst, E. W.: Brain **48**:279, 1925; **49**:36, 1926.

4. Wilson, S. A. K.: Footnote 3, first reference.

5. Hallervorden and Spatz: Eigenartige Erkrankung im extrapyramidalen System mit besonderer Beteiligung des Globus pallidus und der Substantia nigra, Ztschr. f. d. ges. Neurol. u. Psychiat. **79**:41, 1922.

itself, but in the cell bodies of the ganglion cells. Coarse yellow-brown granules were seen in the perivascular spaces contained within phagocytic cells. Throughout the gray and white substance were peculiar swellings of the nerve fibers, most marked in the corpus subthalamicum. Some of the swellings contained granules. The ganglion cells of the entire cortex were greatly decreased. The pallidum gave an almost normal medullary sheath picture.

A family in many respects similar to that of Hallervorden and Spatz was reported by Kalinowsky.[6] The report concerned three brothers who were similarly affected; a sister remained normal. The parents were not related by blood, nor was there evidence of Jewish extraction. Syphilis was not present. The three brothers resembled each other as to facial appearance and build and the symptoms in all of them were as if "with photographic trueness." The onset was between 9 and 10 years, with pes equinus and progressive stiffness of the legs and later also slight hypertonia of the arms. In a year or so visual disturbances developed, with progressive decrease in the psychic sphere. The fully developed picture was as follows: high grade dementia, to complete deterioration; a tendency to involuntary laughter; optic atrophy, especially temporal, with color scotomas and marked visual decrease, still not a complete amaurosis, but with integrity of the macula lutea; severe disturbance of speech, which was characteristically explosive and monotonous; increased tonus in the arms, without paresis; rigidity of the legs in adduction and flexion at the knees; deformity of the feet with a combination of pes equinus, pes cavus and club foot; increased knee reflexes, and an inconstant Babinski sign; incontinence; normal sex power, and increased libido. The picture was completed by extrapyramidal hyperkinetic phenomena which occurred in different forms in the three brothers. In the oldest, in whom a microscopic examination was made, evident hyperkinetic symptoms of an athetoid character occurred in the head and hands; in both younger patients there were tremors of the hands, and in the youngest there was also a severe palilalia. The oldest brother died of intercurrent bronchopneumonia at the age of 26. Macroscopically, the brain showed smallness of the cerebellum and an unusual discoloration of the globus pallidus; the substantia nigra showed bilaterally a brownish-green color, which was more intense than in the pallidum.

Microscopic investigation showed most intense involvement in the pallidum and the zona reticulata of the substantia nigra, of a very similar nature. Here the parenchyma was most severely affected, with marked decrease in the number of ganglion cells; those remaining were

6. Kalinowsky, L.: Familiäre Erkrankung mit besonderer Beteiligung der Stammganglien, Monatschr. f. Psychiat. u. Neurol. **66**:168, 1927.

severely diseased. As end-products of the cell changes there were peculiar granular pictures that were also found by Hallervorden and Spatz,[5] which were considered by them as ballooning out of the axis cylinders. Against this idea were not only the form and size of the globules but the occurrence of transition forms with analogous pigment granules in the ganglion cells, so that the author concluded that the globules were peculiarly degenerated ganglion cells. The entire stroma was overrun with massive deposits of pigment so that both centers were clearly outlined even macroscopically by their dark color. Although most of the deposit gave an iron reaction, some gave a lipoid reaction. The granules were also present in Hortega glia cells and in the adventitial spaces of the vessels and were free in the tissues. In the striatum the large cells were lessened in number and those remaining were severely diseased, while the small cells were pale and shrunken. In all three of the centers mentioned, the glial elements were greatly increased, although there were none of the Alzheimer glia type. The medullary sheath stains showed a status dysmyelinisatus of the pallidum (C. and O. Vogt). The cerebral cortex showed throughout a loss of ganglion cells with increase in glia cells. This was a diffuse change, and at no place was there a focal loss. The motor area was most severely diseased, especially the third and fifth layers. There was likewise severe affection of the third layer of the frontal area. The relative integrity of the temporal and occipital areas was stressed. There was absence of the peculiar fibrillary swellings described by Hallervorden and Spatz.[5] In the cerebellum the Purkinje cells were lessened in number, and those remaining were altered and displaced. In the spinal cord the pyramidal tracts were slightly degenerated. Inflammatory changes were entirely absent. The mesodermic tissue was unaltered.

PATHOLOGIC REPORT OF CASE

Résumé of Pathologic Observations.—A general autopsy, fourteen hours after death, revealed two congenital malformations: a defect of the aortic cusp, and a double coronary artery on the right. There was not the slightest suggestion of cirrhosis of the liver, and the other abdominal organs were normal. Grossly, the brain and cord were normal, except for a peculiar yellowish-brown discoloration of the inner segments of the lenticular nuclei. The brain was cut in the fresh state and study by serial sections was made of the basal ganglia region, most of which was fixed in alcohol; one block from each side was hardened in formaldehyde. The cell pictures were judged entirely from sections of the alcohol-fixed material stained with toluidine blue; any possibility of distortion such as is seen in formaldehyde-hardened tissue was thus eliminated.

A retrograde change in the cortical motor cells had occurred on which little stress is to be placed because of the varying conditions under which this occurs. Stress is to be laid on the fact that, except for the pallida and the pars reticularis of the substantia nigra, the entire brain and cord were within normal limits. It is to be emphasized further that the striatum (putamen and caudatum) showed absolute integrity, not only of the small cells but of the large ganglion cells as well. This is important in view of Ramsay Hunt's [7] conception of the pallidal system. The pathologic process in the pallidum consisted of a severe cell change in which disappearance of the individual neurons occurred, with gradual replacement by lipoid and an iron-staining pigment so that the eventual picture was a globular mass either of lipoid or of an iron pigment or of both. It was noted that the anatomic division of the pallidum into three segments could be used to classify the pathologic changes: the innermost segment adjacent to the internal capsule being the most severely affected, while the outer segment in relation to the putamen suffered the least amount of damage. In the former no structures were to be found that even remotely resembled a ganglion cell, while in the latter the character of the change could easily be made out. The glial reaction was mainly of the astrocytic type.

The changes in the pars reticularis of the substantia nigra were similar in every way to those found in the innermost segment of the pallidum. It was thought that this was a definite substantiation of the embryologic and anatomic work of Spatz [8] in showing that this part of the substantia nigra is really part of the pallidum, having become separated from it by the posterior fibers of the internal capsule. A system selectivity is to be postulated, based on the work of Schaffer [9] of Budapest. No mesodermic or inflammatory reaction occurred.

Details of Pathologic Examination.—A complete gross and microscopic examination of the viscera was carried out. Two developmental defects were found, namely, a defect of an aortic cusp and a double coronary artery on the right. The abdominal organs were carefully examined, and all of them were found to be normal. Particular mention is made of the fact that the liver, spleen and pancreas were normal. Gross examination of the brain showed a terminal thrombosis of the superior longitudinal sinus, with the enormous venous congestion that it produces. On section of the brain, no abnormal ventricular dilatation was noted. The only gross observations were abnormal discolorations of the pallidum and the reticular portions of the substantia nigra. The blood vessels were normal.

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7. Hunt, J. Ramsay: Progressive Atrophy of the Globus Pallidus, Tr. Am. Neurol. A., 1916, p. 104.

8. Spatz, Hugo: Zur Anatomie der Zentren des Streifenhügels, München. med. Wchnschr. **68**:1441 (Nov. 11) 1921.

9. Schaffer, Karl: Ueber das morphologische Wesen und die Histopathologie der hereditaer-systematischen Nervenkrankheiten, Berlin, Julius Springer, 1926.

Microscopic Examination.—The soft membranes of the cortex were thin and contained no abnormal elements. The vessels within the meninges had thin walls. The gray matter in all areas of the brain showed a normal architecture. Most of the ganglion cells were pale but showed no marked defects, except the large motor cells. Most of the latter were swollen and showed a tendency to become round. In the center, the Nissl substance had disappeared, leaving a very fine stippled material. The nuclei had a tendency to migrate peripherad. The process fitted in with what is usually called axonal chromatolysis; this is found under such varied etiologic conditions that no conclusion can be drawn from it. Pearson,[10] in my laboratory, has recently gone into this subject again, following the lead of Adolf Meyer, who called the condition central neuritis. It must be emphasized, however, that this change in the Betz cells was by no means universal. There was no pseudogranular layer. The blood vessels within the gray matter showed no noteworthy changes.

The white matter was practically entirely normal, except for the discovery of an occasional vessel in the adventitial space in which from several to many pigment-laden phagocytic cells were found.

The general make-up of the cerebellum was normal. There was the usual number of Purkinje cells, although their processes were visible for greater distances than is considered normal. There was little or no increase in Bergmann's glial layer. Particular mention must be made of the dentate nucleus, the cells of which were not lessened in number and showed no degenerative manifestations, except possibly slight difficulty in taking the toluidine blue stain. Bielschowsky preparations of the cerebellum were normal.

The medulla and pons could be considered to be within normal limits.

Special mention must be made that the anterior horn cells of the spinal cord were found to be practically normal in all respects with the various staining methods. The pyramidal tracts were also normal with the various stains, especially the Marchi and modifications of the Weigert myelin sheath stains.

The choroid plexus contained a considerable amount of iron pigment, but aside from this was normal.

The striatum (caudate and putamen [Vogt nomenclature]) showed an entirely normal structure; in particular, there was the normal relation between the small and the large cells. The large ganglion cells were sharply marginated, and contained Nissl granules and a normal nuclear structure. The processes were probably a little more evident than is usual, but not enough to be considered abnormal. Small groups of oligodendroglia were occasionally seen about some of the large ganglion cells, but not more than is usual. Small amounts of lipoid were observed in some of these larger ganglionic elements. The small ganglion cells were likewise present in their usual numbers and showed no deviations from the normal. Glia cells were not increased in number or in size. The blood vessels showed nothing of note. Fat stains gave no hint of abnormalities. Special glia stains likewise gave normal results. The iron stain did not show increased iron pigment.

It was in the pallidum that the changes were not only most evident but of such intense degree that they will be discussed in detail. As is well known, the pallidum is divided by the lamella pallidi interna into a pars interna and a pars externa, the former being again divided, through the lamella pallidi accessoria,

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10. Pearson, G. H. J.: Central Neuritis; Its Etiology and Symptomatology, Arch. Neurol. & Psychiat. **20**:366 (Aug.) 1928.

into two segments, so that as a result there are three segments. Because of the differences in intensity of involvement of the three segments, each will be discussed separately.

(*A*) The innermost segment showed the most intense change. Under a low magnification (fig. 1) the picture did not have the slightest resemblance to the normal pallidal structure. Instead of the usual irregularly placed, large spindle cells, one could see a great number of balloon-like structures filled with fine and coarse granules that stained greenish blue in toluidine blue preparations. These globular masses were contained within microglia cells. One could note an occasional mass that still had the form of a ganglion cell. I have seen similar pigment masses in other cases of degeneration of tissue, the latest occurring in a man, aged 77; in this case there was no doubt that the degeneration was the result of a thrombotic lesion. There is therefore nothing specific or characteristic in this type of degenerative change. Other masses of similar size and shape were seen which stained very faintly and had a yellowish-brown coloration in toluidine blue preparations. A finely granular appearance was noted on closer study. These masses were the remains of the ganglion cells. On higher magnification (fig. 2) the differences between the two types of globules could easily be made out. With differential stains one could perceive that the darker masses consisted mainly of iron-staining granules, while the yellowish masses took the lipoid stains. Occasionally, cells were met with that contained both. The glial changes were striking; the entire tissue was overrun with glia nuclei which gave the tissue a very dense appearance. These could be divided into three groups: (1) The most numerous were the glia cells with large irregularly round or oval nuclei, scanty chromatin granules and a cell body that showed feebly in toluidine blue preparations, but with the same type of granules in the cytoplasm as in the ganglion cells. These cells appeared almost similar to those described by Alzheimer in pseudosclerosis, but they were smaller and differed slightly in their morphology; they were not considered to be Alzheimer cells. With special glia stains these cells showed the characteristics of fibrillary astrocytes. (2) Small, round, deeply staining nuclei, without visible cytoplasm with the ordinary staining methods, which with the newer silver stains were made out to be oligodendroglia. (3) Small, irregular, sausage-shaped nuclei which were to be carefully distinguished in toluidine blue preparations from the endothelial cells of capillaries. They were microglia and could be so demonstrated by special stains. There was no increase of blood vessels. Evidences of inflammation were lacking.

(*B*) The mesial segment was less involved than the innermost segment, but it was in this segment that a clue was given as to the change in the ganglion cells. One saw a fair number of bodies that were recognizable as ganglion cells, but not one was normal. They showed an indefinite outline and a tendency to become globular, with entire loss of Nissl substance, and the cytoplasm had a yellowish background (lipoid) with dark greenish-staining granules (iron) at one or both poles and a fine brownish reticulum through the entire cytoplasm. The nucleus was comparatively large, but the outline was not as sharply demarcated as normally. The nucleolus was at times distinct. There were also a few of the masses of greenish granules that stained positively for iron, in all respects similar to those found in the innermost segment. Only occasionally was the greenish pigment scattered through the tissue. There were fewer cells of the type that resemble the Alzheimer glia cells, and much less fibrillar structure than when the Alzheimer cells are present. No new vessel formation could be made out.

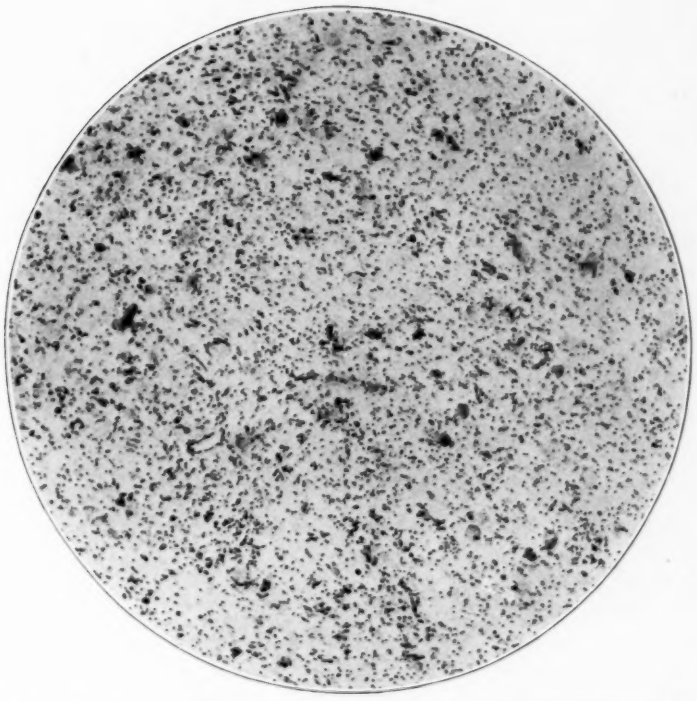

Fig. 1.—The inner segment of the pallidum; intense degeneration showing the absence of all normal structure and the presence of globules of light and dark-staining pigment. Toluidine blue stain; × 80.

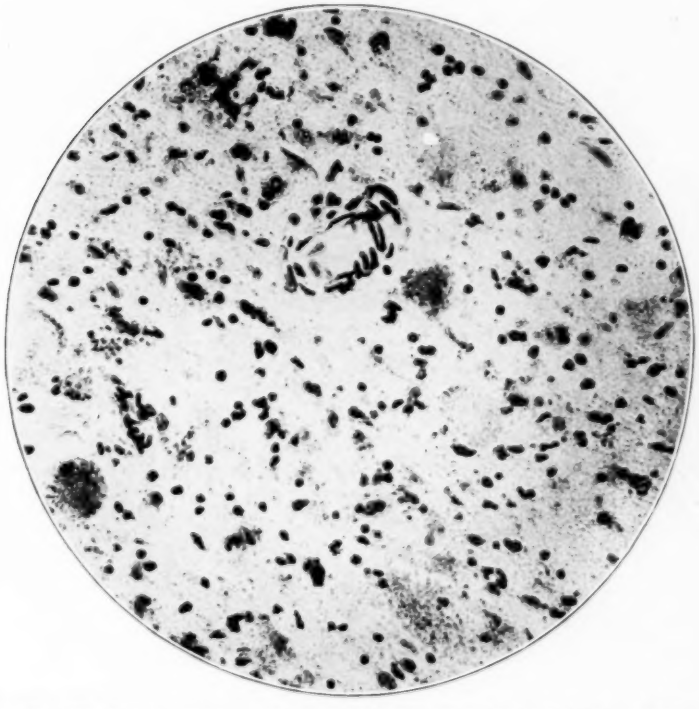

Fig. 2.—The inner segment of the pallidum. The intense degeneration of this part of the pallidum can be easily made out. Toluidine blue stain; × 320.

(*C*) The outermost segment, adjacent to the putamen, showed the least severe changes. Here the architectural make-up of the normal pallidum could be made out, but there were fewer ganglion cells than normally. There was not a single cell, however, that was absolutely normal; most of them showed a lipoid degeneration at least. The least involved cells showed an irregular oval outline with an ill-defined nucleus. The cytoplasm had a definite yellowish tinge, with dustlike remains of the Nissl substance, especially in the perinuclear region. The nucleus itself was large and indistinct, with the limiting membrane in folds. No

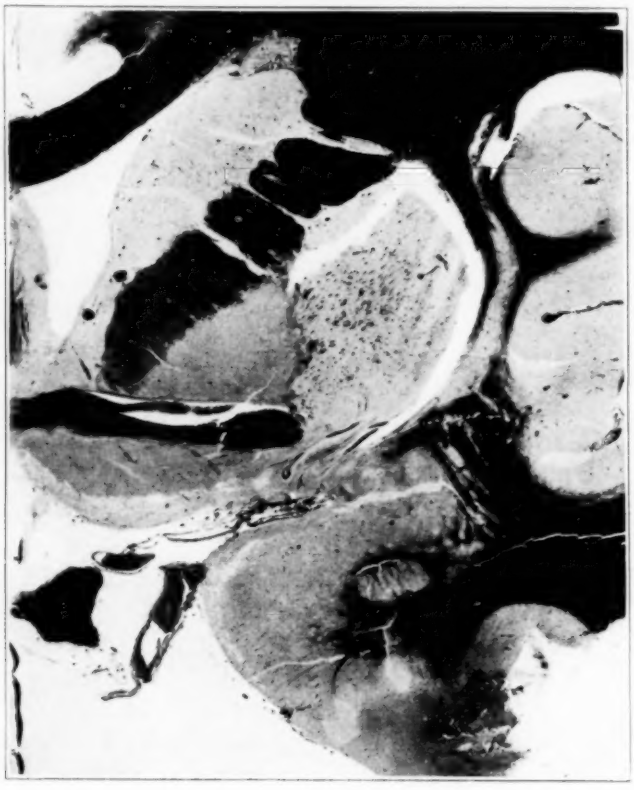

Fig. 3.—A frontal section through the anterior commissure. Normal structure of the striatum as well as of the internal capsule can be made out. An intense status dysmyelinisatus is present. Myelin sheath stain.

evidence of globules of iron granules could be made out. In the cells that were most markedly degenerated nothing was left but an irregularly oval mass of yellowish-brown lipoid pigment.

There were many less glia cells present than in the inner segment; astrocytes and swollen oligodendroglia cells could easily be made out even with toluidine blue stains. There were few or no microglia.

With myelin sheath stains (fig. 3) there was seen a normal striatal picture, while the pallidum was practically completely demyelinized—a typical picture of

status dysmyelinisatus of Cécile Vogt. The internal capsule was normal. The rest of the brain showed a normal myelin sheath picture.

The substantia nigra merits special description. As is well known, it consists of two portions, a zona compacta and a zona reticulata. The former is made up of melanin-containing ganglion cells; in the case under discussion these showed no changes of note. The zona reticulata is almost similar to the pallidum in its structure. It was in the reticular portion of the substantia nigra that changes were encountered. Figure 4 is designed to show the normal structure of the pars reticularis, and to bring out the contrast even more clearly the illustration is taken from a case of intense rigidity following epidemic encephalitis, in which the com-

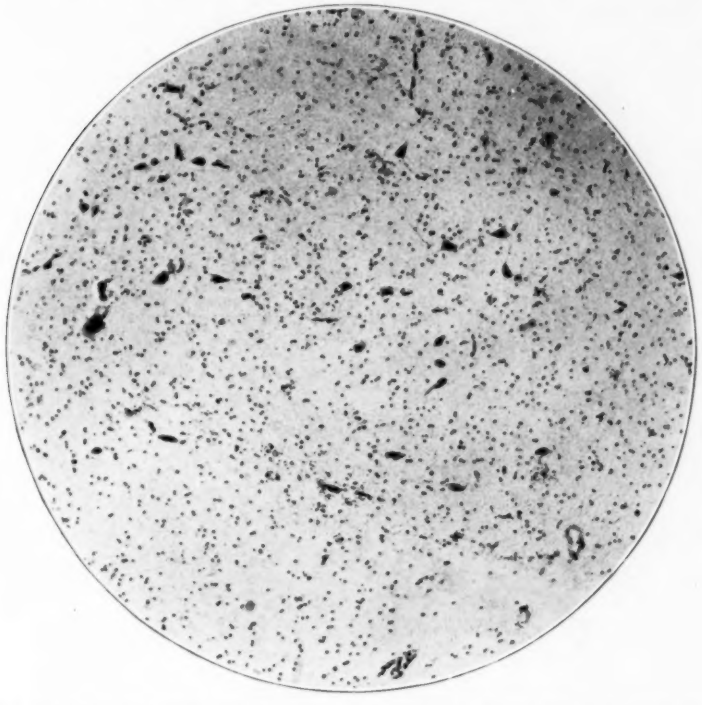

Fig. 4.—The reticular portion of the substantia nigra from a case of post-encephalitic parkinsonism. Comparatively normal structure is present. Toluidine blue stain; × 80.

pact portion of the substantia nigra was completely degenerated. In figure 5, taken from the reticular portion of the patient whose case is described in this paper, it is seen, even under a low magnification, that there was complete absence of normal cellular elements with occasional residuals of globules of iron and lipoid pigments exactly as in the pallidum. This was clearly brought out under a higher magnification (fig. 6); in this way the striking similarity to the condition observed in the pallidum could be made out.

Special stains for iron showed vividly the enormous increase of the iron pigment in both the pallidum and the reticular portion of the substantia nigra. This is brought out in figure 7.

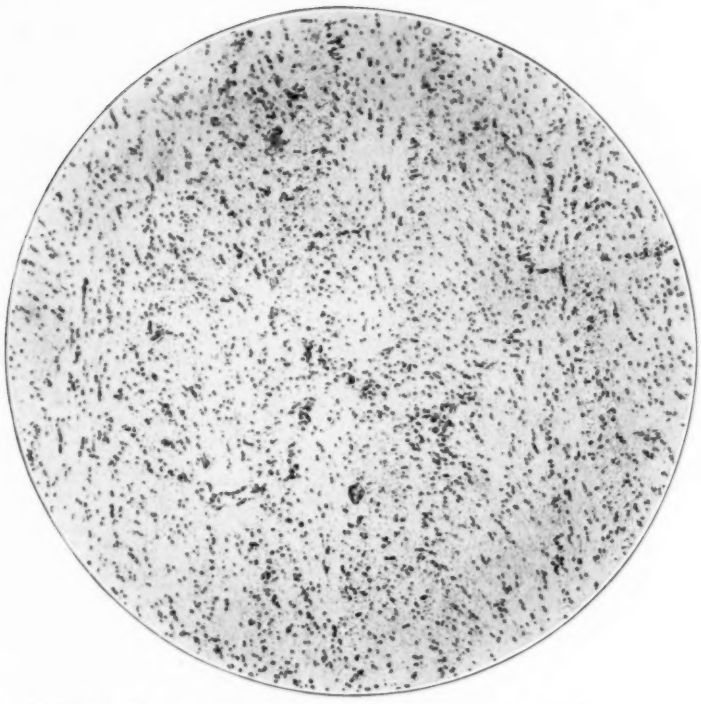

Fig. 5.—The reticular portion of the substantia nigra from the case described. Complete absence of normal cells as well as replacement by globules of pigment can be made out. Toluidine blue stain; × 80.

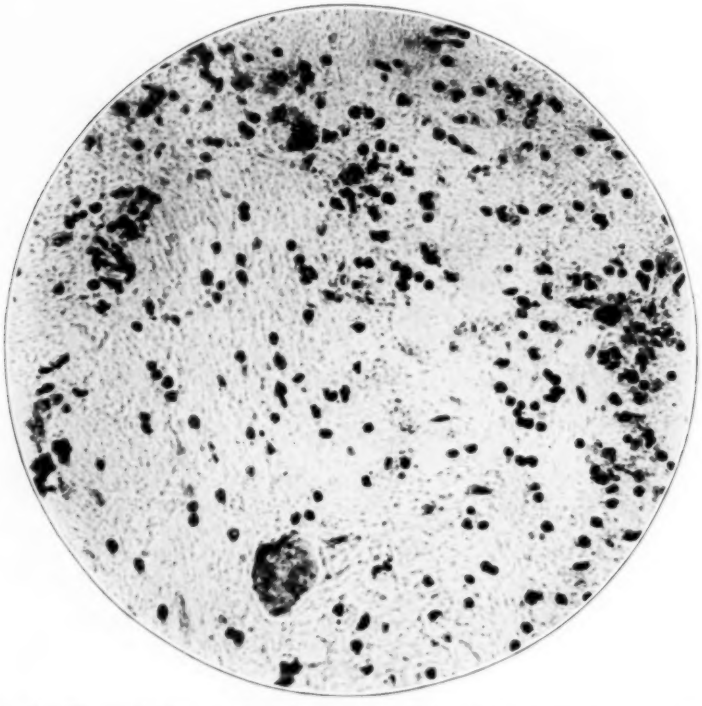

Fig. 6.—The reticular portion of the substantia nigra from the case described in this paper. The similarity of the picture with that of the pallidum is striking. Toluidine blue stain; × 320.

It should be emphasized that other portions of the central nervous system were also carefully examined by the same methods and found to be normal. Particular mention should be made of the fact that the red nuclei and the subthalamic bodies were normal.

Unfortunately only that portion of the retina adjacent to the optic nerves was removed, and this showed little or no change in the retina, but a plastic choroiditis with changes in the blood vessels and an excess of pigmentation were present. This agrees with the clinical observation of pigmentation only around the periphery of the retina.

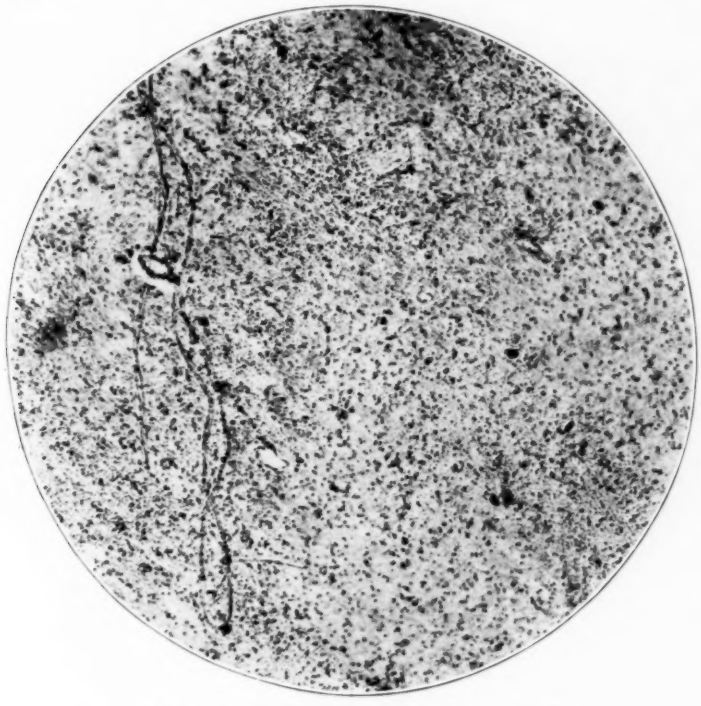

Fig. 7.—The pallidum. Iron stain; × 80.

PROGRESSIVE PALLIDAL DEGENERATION

Because of the great rarity of this disease and its importance in helping to elucidate one of the most complicated and least understood group of structures in the brain—the basal ganglia—I shall give a brief summary of the condition as I have interpreted it.

There can be no doubt that in my case, even more than in the cases described by Hallervorden and Spatz,[5] and Kalinowsky,[6] there was involvement of only the pallidum and the reticular portion of the substantia nigra. This involvement was so limited that it might afford a means of arriving at the symptomatology of this limited portion of the central nervous system. It was thought for this reason that it

might be used as a means of arriving by elimination, eventually, at a conclusion as to the real physiology of the other gray basal structures.

For the condition in which the involvement is limited entirely to the pallidal system—the pallidum plus the reticular portion of the substantia nigra—the name progressive pallidal degeneration is suggested as best expressing the clinical and pathologic features and differentiating the disease from the progressive lenticular degeneration of Wilson, in which the putamen is chiefly affected.

Definition.—Progressive pallidal degeneration may be defined as a systemic disease involving the pallidum and reticular portion of the substantia nigra, bilaterally, characterized clinically by progressive rigidity, beginning early in life. It is familial and may be associated with other hereditary and familial defects, such as retinitis pigmentosa, as in the cases described. Emphasis is to be laid on the facts that tremor is completely absent, and that there are no pyramidal tract signs. The liver and the other abdominal organs are uninvolved.

While in my patients progressive loss of vision marked the onset, this need not necessarily be so. The disease may, on the other hand, begin with rigidity, at first in the lower limbs, and may simulate for a time "spastic" paraplegia. Careful examination, however, soon determines that there are no pyramidal tract signs. Eventually there is involvement of the entire body, including the face.

Etiology.—The etiology, as in all familial and hereditary conditions, is obscure. Consanguinity of the parents is often blamed; syphilis in the ancestors may play a rôle; trauma and infections are to be considered. Gowers' abiotrophy may be but a convenient name to apply to similar conditions when one is not sure of the underlying basis; it may, however, signify an inborn lack of endurance of certain structures, with a tendency to premature decay. No one can deny that in certain families opacity of the lenses may occur prematurely; in other families premature arteriosclerosis develops. These represent a premature "wearing out" of nonvital structures, in contrast to the "wearing out" of some vital organ with resultant death of the entire organism. It is possible to have structural defects in the nervous system also, the best known of which is progressive spinal muscular atrophy in which the anterior horn cells are involved as an entire system in the premature decay. Gowers' term has this particular significance.

Symptomatology.—The symptomatology is comparatively simple and consists of an intense rigidity of the extrapyramidal type, without pyramidal tract symptoms. In the cases described in this paper the rigidity first manifested itself in the lower limbs and progressed upward. The method of onset and progression, therefore, differs from the usual course of events in Parkinson's disease, in which the condition may

begin unilaterally or may remain confined to one limb for a while. This differentiation is important, because in the developed condition there is a marked similarity to the postencephalitic form of parkinsonism, with which progressive pallidal degeneration has been confused. Progressive blindness may initiate the symptoms, as in my case, and retinitis pigmentosa may be the underlying cause for the ocular symptoms. Defective development of other structures may be present, along with premature decay of certain organs. Stress is again laid on the fact that tremor and involuntary movements of all sorts are absent; they remain absent when the symptom complex remains pure.

In the cases reported by Kalinowsky, he mentioned an "inconstant Babinski sign," and pathologic examination did show "lightness of staining" of the pyramidal tracts. It has been my experience that, even in cases in which microscopically the pyramidal tracts have been uninvolved, the clinician, at times, has been suspicious of a Babinski sign. This has occurred particularly in cases of illuminating gas poisoning in which the pallida alone have been involved.

In the cases described in this paper there were no involuntary movements, in contrast to the cases of Hallervorden and Spatz[5] and Kalinowsky.[6] This would make my cases much "purer" than those formerly described.

Differential Diagnosis.—The first condition from which this disease is to be differentiated is juvenile paralysis agitans of Ramsay Hunt, the symptoms of which, according to Hunt,[7] consist of progressive paralysis, rigidity and tremor. The process begins with a rhythmic tremor and rigidity in one limb, which gradually extend to other portions of the body but as a rule involve the limb on the same side before there is a spread to the other side of the body. In the early stages the tremor is often coarse and may become violent during emotion or motor activity. According to Hunt, there has never been a case of this sort in which tremor did not occur at some stage of its course. While this condition may be familial, as in many of the cases reported, it may be difficult to distinguish it from the postencephalitic variety, since even in typical postencephalitic cases there may be no history of an acute attack, although some have been bold enough to suggest that even the cases of juvenile Parkinson's disease occurring before the epidemic of encephalitis were postencephalitic. Dr. Spiller has shown me sections from a patient whom he saw clinically in consultation ten years before the outbreak of encephalitis; in these sections were the typical changes of what is now known as epidemic encephalitis. Had that patient recovered from the acute manifestations and developed Parkinson's syndrome, he would have been considered an "idiopathic" type, and little stress would have been placed on an acute illness months or even years before.

The cases that resemble those of my patients more closely are those of Hallervorden and Spatz,[5] and Kalinowsky [6] already cited. It need be emphasized only that the cases reported in both these contributions were entirely similar clinically, but had the additional features of involuntary movements of various sorts and pyramidal tract signs. These symptoms are explained pathologically by a wider involvement than was present in my case, and this was found by the authors.

Two other cases in the older literature bear a resemblance to my case, but neither was apparently familial. The first case was reported by Rothmann.[11] It was that of an apparently normal child who was slow in walking and talking. From the age of 6 years, there developed "spasticity" with choreo-athetoid movements. At 12, the child died. Even macroscopically shrinkage and discoloration of the pallida were seen. With Weigert stains there were seen numerous sclerotic foci in the pallida, with integrity of the putamen and caudate. No mention was made of the reticular portion of the substantia nigra. No staining methods were used that could give a good picture of the cellular changes.

The second case was that of Fischer,[12] which was similar in all respects to the foregoing one. The symptoms appeared between the ages of 15 and 17, with death at 21. In this case also the pallida were shrunken and dark. Histologically, Fischer found a chronic progressive destructive process of the ganglion cells and fibers, with chalklike particles in the pallida. Again the substantia nigra was not carefully examined.

Pathology.—The underlying lesion is a destruction of the pallida and of the reticular portions of the substantia nigra. As a result of this destruction, the ganglion cells become reduced to globules of fatty particles. There are observed also irregularly oval and circular masses of an iron-staining pigment. Inflammatory evidences are lacking. It is to be stressed that the same type of pigment masses has been found by me in other destructive lesions, coming probably from the blood stream. The entire tissue is overrun with glia cells of both macroglial and microglial types.

Anatomically, the pallidal system is here considered to be made up not only of the globus pallidus, or pallidum, but also of the reticular portion of the substantia nigra. This confirms the work done especially by Spatz.[8] The supra-optic ganglion of Meynert was probably slightly involved in my case, and probably also belongs to this system. In this system there were eventually a complete destruction of the ganglion cells and their replacement by globules of lipoid, with the presence of

11. Rothmann, quoted by Jakob, A.: Die extrapyramidalen Erkrankungen, Berlin, Julius Springer, 1923, p. 283.

12. Fischer, O., quoted by Jakob (footnote 11).

an iron-staining pigment in the phagocytic cells. Myelin sheath stains showed a status dysmyelinisatus, following the nomenclature of Cécile Vogt, a condition that she found in some cases of extrapyramidal rigidity resulting from birth conditions. Particular stress is laid on the complete preservation in my case of the striatum and the other basal ganglia, in both the thalamencephalon and the mesencephalon. Special attention is directed to the fact that the large cells of the striatum, which Ramsay Hunt included in the pallidal system, were normal, and, if this case follows Karl Schaffer's dictum that hereditary diseases exhibit a system selectivity, they are not to be considered part of the pallidal system.

Diagnosis.—The presence of retinitis pigmentosa beginning in early life, gradual progress to blindness, progressive rigidity of an extrapyramidal type, beginning in the lower limbs but eventually involving the entire body, without pyramidal tract signs, and familial occurrence make a distinctive clinical picture.

The absence of retinal and optic nerve changes need not necessarily mitigate against a diagnosis of involvement of the pallidal system. Only recently I have had the opportunty of studying, through Dr. McConnell's kindness, two brothers in the Philadelphia General Hospital who had previously been considered as presenting atypical forms of the postencephalitic syndrome. Both showed "parkinsonian rigidity," but in both the condition had begun early in life and at practically the same age, and became progressive; in the elder brother it had already involved the entire body with the most marked extrapyramidal rigidity in the lower limbs. There is no doubt that many neurologists at present would make a diagnosis of a postencephalitic condition in these two cases, but the onset at about the same age in the two brothers, the marked similarity of the pictures, the absence of the common features of postencephalitis, such as salivation, seborrhea, tremors, oculogyric crises and, what is many times extremely important, the history of an acute encephalitic attack, and in children the complete absence of behavior difficulties are sufficient to eliminate an encephalitic condition.

The development of involuntary movements would signify the involvement of structures outside the pallidal system and would place the case in the group described by Hallervorden and Spatz [5] and Kalinowsky,[6] and not in my group.

Prognosis.—The prognosis is entirely unfavorable; cure is not to be expected, and arrest or remission is a remote possibility. The progress, however, is so slow that the condition may last a long time.

PHYSIOLOGIC CONSIDERATIONS

A presentation of this sort is of value only when it can be applied directly to the clinic, so that physiologic theorization is, at least, per-

missible, even on the basis of two cases, in only one of which the results of autopsy are given.

It is practically universally agreed that the pathologic changes of Huntington's chorea are mainly in the striatum (putamen and caudate) and cortex, the latter accounting for the mental symptoms and the former for the irregular movements. Some of the cases of chronic chorea without mental symptoms have shown disease of the striatum without involvement of the cortex (Jakob[13]). Recent cases of hemichorea have aided the study of the functions of various portions of the basal ganglion system in the presence of an intact cortex, in contrast to the recent views expressed by Wilson.[14] The recent studies on the corpus luysii might be mentioned to show the effect of small lesions in which hemiballismus or severe chorea has been described.

As far as the pallidum itself is concerned, it is well known that in carbon monoxide poisoning there may be involvement of the inner divisions of the lenticular nuclei without disturbance in other parts. In these cases there results clinically an intense rigidity without abnormal movements. The history alone will distinguish these cases also from a postencephalitic condition. With involvement of other portions of the nervous system, such as occurs in many cases of carbon monoxide poisoning, the clinical picture may be greatly modified. In paralysis agitans of the so-called idiopathic and of the postencephalitic types, as shown by many observations, there is usually such extensive involvement of the entire basal ganglion region, as well as of the cortex, that to speak of the condition as a pallidal syndrome or a substantia nigral syndrome is erroneous; any deductions from these observations as to the functions of individual structures in the basal ganglion region are misleading.

One of the most interesting cases from a physiologic point of view was one of chronic progressive chorea occurring after an attack of acute rheumatic fever, in which marked rigidity eventually developed.[15] Not only was the striatum involved in this case, but the pallidum and the reticular portion of the substantia nigra.

The symptomatology given by me for the "pallidal system," with rigidity as the only sign, is contrary to what is found in the literature and does not fit in with Foerster's elementary components. One usually speaks of rigidity and tremor as the common signs of parkinsonism. That they are separate and distinct symptoms is attested by the fact that even in the postencephalitic variety tremor may be completely

13. Jakob, A.: Die extrapyramidalen Erkrankungen, Berlin, Julius Springer, 1923.

14. Wilson, S. A. K.: Modern Problems in Neurology, New York, William Wood & Company, 1929.

15. Jakob (footnote 13, p. 70).

absent. In patients having both rigidity and tremor, one finds that external stimuli can affect the tremor, while the rigidity is not altered. In the case reported by Leriche, in which bilateral section of the fifth, sixth and eighth cervical posterior roots was done, the tremor diminished but the rigidity is said to have remained unaltered.

One must not overlook the effects of various drugs in the elucidation of this extremely complicated problem. It is well known that the scopolamine compounds can markedly affect the rigidity in paralysis agitans while the tremor remains unaltered. This is certainly suggestive of a dissociation of the symptom of tremor from that of rigidity. It must be kept in mind that in my case, with involvement of only the pallidal system, tremor was completely absent, while in the usual case of paralysis agitans there is involvement of the entire central nuclear masses, and the resulting syndrome is tremor with rigidity. The studies of Walshe [16] have been used in arguments for and against the various theories as to the relation of the two predominant symptoms of tremor and rigidity. Following the injection of small quantities of a 1 per cent solution of procaine hydrochloride into the motor point of the biceps brachii, Walshe observed no appreciable reduction of the tremor or rigidity, but if larger quantities were used the rigidity was entirely abolished while the tremor remained unaffected. With the injection of still larger quantities of the solution, all reflex and voluntary movement of the muscle was destroyed. Byrnes,[17] in his excellent work on the pathologic changes observed in the muscle spindle in paralysis agitans, was inclined to discredit this study completely and stated that "the conditions of the experiment did not warrant Walshe's conclusions that 'tremor is unaffected by de-afferenting the tremulous muscles and cannot, therefore, be a proprioceptive reflex.'"

The work done on bulbocapnine in paralysis agitans and in other tremor states has shown that under certain conditions there may be a distinct lessening of the tremor while the hypertonicity remains unaltered (de Jong and Schaltenbrand,[18] Lewy,[19] Leiner and Kaufman [20]). While experimental evidence, as outlined, is in favor of the independence of

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16. Walshe, F. M. R.: Observations on the Nature of the Muscular Rigidity of Paralysis Agitans and on Its Relationship to Tremor, Brain **47**:159 (May) 1924.

17. Byrnes, C. M.: A Contribution to the Pathology of Paralysis Agitans, Arch. Neurol. & Psychiat. **15**:407 (April) 1926.

18. de Jong, H., and Schaltenbrand, G. S.: Die Wirkung des Bulbocapnin auf Paralysis agitans und andere Tremorkranke, Klin. Wchnschr. **3**:2045, 1924.

19. Lewy, F. H.: Erfahrungen über die Wirkung von Bulbocapnin auf das Zittern, Deutsche med. Wchnschr. **52**:351, 1926.

20. Leiner, J. H., and Kaufman, M. R.: Bulbocapnine in Diseases Manifesting Dyskinesia, Arch. Neurol. & Psychiat. **20**:1269 (Dec.) 1928.

tremor and rigidity, the outstanding evidence, however, is the occurrence clinically of rigidity without tremor and at times marked tremor with but little rigidity.

The question of localization of the body segments within the pallidum should be touched on, but one does so with considerable trepidation, especially on the basis of a pathologic study in only one case. Since the investigations of Mingazinni and C. and O. Vogt, somatotopic localization within the striatum has been considered likely but is still far from general acceptance in view of the widely divergent symptoms resulting from lesions in apparently similar locations. At present one can say only that while localization is probable, it has not yet been proved. One sees focal striatal symptoms clinically, such as irregular movements of a choreic nature, limited, for example, to only a part of a limb, but cases of this sort have not been carefully studied anatomically.

The supposed localization within the striatum has simply been carried over to the pallidum, as the motor localization in the cortex is carried over to the sensory area. But in the light of the difference of phylogenesis and ontogenesis, it is probably far from similar. Pure focal lesions of the pallidum have not been described, yet it is known clinically that even the symptoms of paralysis agitans may begin in one limb and may remain localized to that limb for a long time.

It has occurred to me as a result of the study of the case herein reported that perhaps the division of the pallidum is not like that of the striatum, in which the anterior part is supposedly in relation with the head and so on, but that, as brought out particularly by the Vogts, the pallidum is made up of three segments arranged in a quadrantic manner adjacent to the internal capsule. One must make the suggestion cautiously, and it is only a suggestion, that these three segments might be in relation to the three body segments. This suggestion was made several years ago at a pathology conference and was not accepted, but since that time Schilder and Stengel [21] have come to a similar conclusion in a case of tabes with athetoid movements. It may be a circumstance only, but in my case the rigidity first involved the lower limbs and was greater there than in the rest of the body. It might prove significant that pathologically the involvement was greatest and most intense in the small inner apical segment adjacent to the internal capsule, while the outer segment, in relation to the putamen, was the least involved.

One naturally can make no sweeping generalization on the basis of one case, and this idea is recorded in the hope that future investigations may either prove or disprove the statement.

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21. Schilder, P., and Stengel, E.: Ueber athetotische Bewegungen bei Tabes dorsalis, Ztschr. f. d. ges. Neurol. u. Psychiat. **113**:613, 1928.

SUMMARY AND CONCLUSIONS

1. Two cases with an unusual syndrome are described, occurring in brothers, in one of whom a pathologic study of the nervous system was made.

2. For this syndrome the name progressive pallidal degeneration is suggested. It consists of a progressive rigidity that begins in the lower limbs and eventually involves the entire body. In my patients, retinitis pigmentosa was present as evidence of a familial condition.

3. Pathologically, the same sort of involvement was present in the pallidum and in the reticular portion of the substantia nigra.

4. The case in which a pathologic study was made further advances the idea that the pallidum and the reticular portion of the substantia nigra are phylogenetically and ontogenetically similar.

5. The name "pallidal system" is suggested for these two structures.

6. It is thought that rigidity without tremor may be the only clinical manifestation of involvement of the pallidal system.

CERTAIN FUNCTIONS OF THE ROOTS AND GANGLIA OF THE CRANIAL SENSORY NERVES *

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The continued use of the subcerebellar route for section of the posterior root of the trigeminal nerve in tic douloureux has led to observations that, I believe, offer evidence that the gasserian ganglion mediates a definite function which in large degree modifies the afferent sensory impressions en route to the brain. Doubtless, what holds true for the trigeminal ganglion is equally pertinent for the ganglia of the other cranial nerves carrying sensory stimuli of the same character. Doubtless, too, comparative modifications of function, though of altered character dependent on differing afferent functions, likewise exist for other sensory ganglia.

The data of experimental character are in large part derived from subtotal sections of the sensory root of the nervus trigeminus. Obviously there is almost no opportunity of making or even of testing such experimental observations in animals. From a series of approximately 200 cases, partial section of the root in varying degree was performed in about 150 instances. It will be recalled that the sensory root is divided alongside the pons, usually at a point about 0.5 cm. from the attachment to the pons.

The first results having a bearing on this problem are derived from section of the posterior half of the sensory root. They are as follows: 1. There is almost no loss of sensation that is demonstrable objectively or that is appreciable subjectively by the patient. 2. The characteristic pain of tic douloureux is permanently abolished. 3. Cure of the pain appears to be obtained regardless of the peripheral branch or branches involved. Whatever interpretation may be placed on these results, one at least feels safe in making the following deductions: 1. There is no accurate subdivision of the sensory root into three anatomic subdivisions corresponding to the peripheral branches of the nerve. In other words, there is either a topographic rearrangement of the fibers or a change in their character, or perhaps both. 2. Since the pain is cured in all

* Submitted for publication, June 16, 1931.

* From the Johns Hopkins University and Hospital.

* Read at the Fifty-Seventh Annual Meeting of the American Neurological Association, Boston, May 28, 1931.

divisions by dividing a selective part of the nerve, there must be, in some degree at least, a distribution of fibers according to function in the sensory root.

The next results are obtained from more extensive partial sections (two-thirds or three-fourths or more) of the sensory root. Sensory changes, both subjective and objective, now develop, though proportionately less than the degree of section would lead one to expect: 1. In the loss of sensation there is, in some degree, preservation of the peripheral topographic arrangement of fibers, but it is always imperfect and never approaches accuracy. Moreover, the results are far from consistent. When sections are made in the sensory root from the posterior to the anterior border, there is, on the whole, greatest loss over the sensory domain of the inferior peripheral branch of the nerve, next of the middle portion and lastly of the ophthalmic division. But the peripheral sensory changes may be greater over the second or even over the third mentioned division than over the inferior branch, although the order of section of the nerve is unchanged. 2. Rearrangement of fibers according to function is now always in evidence; this functional arrangement is imperfect and is never so complete as in the foregoing experiment in which the pain was so selectively concentrated in the lower half of the nerve. Frequently, one finds loss of one type of sensation over the domain of part or all of two or three peripheral branches when another sensation or other sensations are intact or nearly so. For example, the perception of heat and cold may be lost over the second and third divisions when perception of a light touch is preserved; perception of touch may be preserved over a large part of all three divisions when other sensations are absent, or sharpness and dulness and touch may be appreciated over the second and third branches when heat and cold are not differentiable.

The next observations are on the character of the pain of trigeminal tic douloureux. They indicate that this characteristic pain is distinctive of a condition of the sensory root and is not obtainable from any lesion of the peripheral nerves. If this is true, there is evidence of another kind that the gasserian ganglion mediates a function and is not merely a way station through which sensory impressions pass intact.

In this series of 200 cases, 10 neoplasms were found. All were small and merely impinged on the nerves. There were no clinical differences in the character of the pain and no objective disturbances in the sensory area. In other words, the pain was precisely similar to that of so-called idiopathic tic douloureux. On the whole, perhaps the pain was consistently referable to more than one branch of the nerve, but this is by no means a characteristic differential point. This percentage of incidence

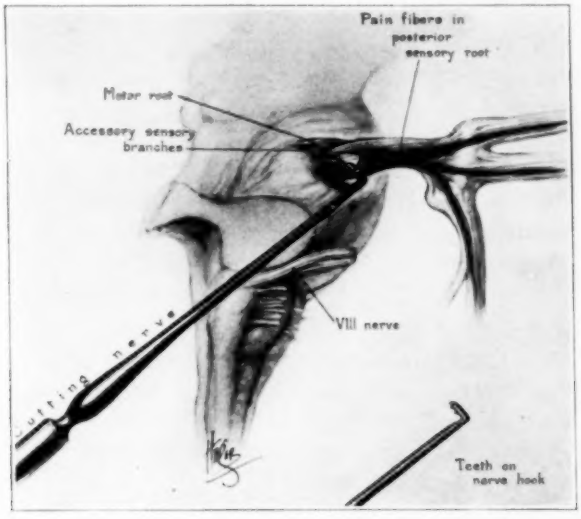
of neoplasms (5 per cent of the total number of cases) is certainly too high to be explained by coincidence. In addition to the actual growths, in an equal number of cases the sensory root was surrounded by an angiomatous mass of congenital origin, which unquestionably was responsible for the pain. In another group of about 10 or 15 per cent of the cases, the trigeminal root was permanently bent on itself at a sharp angle by an underlying artery or a large branch of the petrosal vein. The cause of the pain in these cases appears to be equally relevant. But even if the last two groups are excluded, because proof of such character has not hitherto been offered, the group of neoplasms alone is adequate to establish one kind of gross causative relationship to the characteristic pain. That these three types of gross lesions have not been recognized is, of course, due to the fact that Krause's temporal approach, which is almost universally used, has not exposed the sensory root.

In contradistinction to the microscopic observations cited, it can be stated without, I think, danger of error that a lesion of any kind along a peripheral nerve has never been found to cause tic douloureux. Pain produced by a peripheral lesion is always of a different character—it is steady and persisting and never so excruciating, and follows the involved peripheral branch to its terminations; in other words, it is not of paroxysmal type. It would therefore appear to be inevitable that the pain of tic douloureux is due to involvement of tracts of a higher sensory level and must be in the sensory root. I am prepared to believe, but not absolutely to prove, that tumors of or involving the gasserian ganglion (exclusive of the sensory root) also do not cause pain of this paroxysmal type. In perhaps a dozen personally observed cases with tumors in this region, the pain has never been of ticlike character. At least the differences between the pains arising from the peripheral branches and the sensory roots leave no doubt that the interposed ganglion has entirely changed the character of the pain.

It has long been reasoned that the pain of tic douloureux must arise in a peripheral branch of the nerve, because the pain is so sharply restricted to a single branch in so many cases and peripheral division stops the pain until restored by regeneration of the nerve. A superficial analysis of the pain will show that a peripheral stimulus could not produce a pain of this kind, because it does not cover the domain of the nerve. Although the pain is referred to a particular branch, it does not spread over the peripheral terminations of the branch. Rather it may jump to another branch or branches and yet may not spread locally. The course of the pain and the rough degree of its localization are due to the fact that the origin is in the sensory root. This degree of localization in the sensory root is about what one would expect

from the experimental evidence already presented. The detailed and comprehensive sensory distribution of pain has been lost in the gasserian ganglion.

It is my belief that paroxysmal pain of the type observed in the trigeminal and glossopharyngeal nerves is just as positive evidence of origin in a higher sensory level as a clonic convulsion is evidence of origin in a higher motor level. And just as one cannot produce a clonic convulsion by a lesion on or stimulation of a peripheral motor nerve, so one cannot produce a paroxysmal pain by a lesion of a peripheral sensory nerve.



Concentration in the sensory root of the fibers responsible for the pain of tic douloureux.

One other chance observation on a sensory cranial nerve appears to lend support to, and perhaps to amplify, these conclusions. During an operation on a hypophyseal tumor, the right optic nerve was accidentally divided through somewhat more than half of its transverse extent when the line of vision was momentarily obscured by the handle of a curet. The cut in the nerve was oblique, and extended anteriorly and outwardly for a distance of about 1 cm. from a point on the inner side of the nerve, about 2 mm. anterior to the chiasm. Anteriorly, the cut extended somewhat beyond the midline of the nerve.

Prior to operation, the patient had shown a bitemporal hemianopia for form and color in each eye. The visual acuity was slightly less on the side of the operation (right). Forty-eight hours after the operation, the fields of both eyes had in large part returned, and before the

patient left the hospital, two weeks later, repeated perimetric tests by different examiners gave normal fields for form and color in both eyes, and the visual acuity was normal. There was no scotoma. Not the slightest defect of vision could be detected in the affected eye at any time.

These negative findings have indeed caused me to wonder if my observation of a sectioned optic nerve may not have been at fault, even despite the fact that I picked up the overhanging fragment of nerve and replaced it in its natural position. The nerve was not traumatized by sponging. Being greatly distracted by the accident and the seeming certainty that total blindness of that eye would result, I saw no need of having my assistant check the observation, so it must remain unsupported. It is difficult to believe that I could have been mistaken in such a simple observation, particularly since the optic nerve is always in full view and is the all-important landmark.

To test the results as far as possible, an experiment was made on a dog as follows: The outer half of the left and the inner half of the right optic nerves were sectioned immediately in front of the chiasm. Several days after the operation, the dog was tested by rapid movement through a narrow irregular path. Although a right homonymous hemianopia would have been the expected result of the experiment, the dog rapidly negotiated the path through the laterally placed impediments on either side with perfect ease. Although the animal was tested repeatedy, there was no tendency to run into objects on the side on which blindness might have been expected. Although the result in this canine experiment apparently harmonizes with the negative human result, there still remains a doubt, because the dog may be able to compensate for loss of vision by rapidly shifting the eyes and neck. On roughly testing the fields of vision by thrusting an object toward the eye, vision seemed to be unaffected; but in this respect again the test is too crude to be dependable. As a matter of fact, the negative results of hemisection of the optic nerve are almost precisely similar to those attending hemisection of the trigeminal nerve. It is realized that these results, if correct, are difficult if not impossible to harmonize with an inflexible neuron doctrine.

ABSTRACT OF DISCUSSION

Dr. Israel Strauss, New York: As I understand it, Dr. Dandy has performed this operation in about 200 cases. Has he had the experience that other neurosurgeons have had following the Frazier-Spiller operation, i. e., persistence of pain in the distribution of the trigeminal, which they are unable to relieve or to explain?

Secondly, Dr. Dandy recently had a patient from New York on whom he had performed this operation. Although the woman was relieved for quite a long period of time, there was recurrence of the pain in part of the trigeminal region:

he reoperated, and up to the time of this report she has been free from pain. At the time of the recurrence she began to complain of some pain in the other trigeminal distribution, and Dr. Dandy, believing that that was indicative of involvement of the other nerve, performed a similar operation on the other side. Now, in view of the rarity of bilateral involvement of the fifth nerve, what induced Dr. Dandy to operate on the other side? What in his experience caused him to predicate the fact that subsequently the patient was to have a real involvement of the sensory root on the other side? She experienced particular discomfort because she was unable to chew and to hold her false teeth — not that her masseter muscles are involved, but because of impairment of sensation in the lips and mouth. She has had to relearn the art of chewing, but she has done so, and is now in excellent condition.

Dr. J. Ramsay Hunt, New York: In making the sensory tests, did you use the necessary care in testing epicritic sensibility? It seems to me that it would be most important in studying the sensory disturbances of such a partial root section to test for the finer alterations of function of epicritic sensibility.

Dr. Wilder Penfield, Montreal: Is it spontaneous pain only that disappears or is it the capacity for feeling pain, and are all three divisions similarly affected? Are the corneal reflexes also preserved? It seems to me that there are many advantages in Dr. Dandy's approach. I, for one, have never undertaken it, and I should like to know about the details.

Dr. C. A. Elsberg, New York: A possible explanation for the preservation of cutaneous sensibility, excepting that for pain, over the distribution of the trigeminus after the subtotal or partial division of the posterior root near the pons may be given on the basis of the research of Dr. S. W. Ranson and others. As is well known, Dr. Ranson has demonstrated that in the posterior spinal roots near the cord, the fine myelinated and unmyelinated fibers that carry the sensibility of pain are grouped together and enter directly into the zone of Lissauer and from there into the substantia gelatinosa of Rolando. Although the trigeminal root does not contain many unmyelinated fibers, a large number of fine fibers that carry the sensation of pain are grouped together in the posterior part of the sensory root of the trigeminus near the pons. These fibers do not divide into branches that pass both upward to the main sensory nucleus and downward, but run directly downward into the spinal tract and the spinal nucleus of the trigeminus. The coarser fibers in the trigeminal root divide into small branches which pass upward and larger fibers which pass downward, and these probably transmit tactile and other sensations, but it is the fine myelinated fibers that pass directly downward that in all probability carry the sensation of pain and possibly that of temperature. It seems to me probable, therefore, that in the patients in whom Dr. Dandy found, after the partial division of the trigeminal root near the pons, a preservation of tactile sensibility with a loss of sensibility to pain, an adequate explanation is that he happened to divide the bundle of fibers carrying sensibility to pain from all parts of the face which passed into the pons and directly downward into the spinal cord. In this connection it should be noted that the spinal tract of the trigeminus is a direct continuation of the zone of Lissauer in the spinal cord, and the spinal nucleus of the trigeminus an upward continuation of the substantia gelatinosa of Rolando.

Dr. Harvey Cushing, Boston: I have had considerable personal experience with operations in the chiasmal region, and I find it very difficult to believe that division of fibers in the optic nerve will fail to cause corresponding field defects.

On the other hand, I have had no experience whatsoever with these trigeminal neurectomies via the posterior cranial fossa, for my associates and I still use the temporal route and divide the entire nerve root.

With his novel method of approaching the root, Dr. Dandy has evidently hit on something of great physiologic interest and importance. It is very extraordinary that the subjective sense of pain should be abolished by incomplete division of the root near the pons and that complete preservation of sensitivity to pain should at the same time remain in the trigeminal skin field.

I would like very much to ask him whether he has at any time, by accident or intent, divided the opposite side of the nerve, leaving this lower portion untouched. One would suppose from his studies that such a procedure as this would render the trigeminal skin field anesthetic to painful, thermic and tactile stimuli, the tic douloureux meanwhile remaining unaffected. If he has not done so, it seems to me that it would be a test worth carrying out as a control; and should the patient's attacks of pain continue under these circumstances, in his skilful hands the completion of the neurectomy at a subsequent session would offer no difficulty.

If, as he suggested, pressure against this portion of the nerve root may in some cases be a cause of pain, why do acoustic tumors, which inevitably press on the trigeminal nerve root, not more often cause facial neuralgia?

Dr. Dandy: I had not intended to discuss the clinical side of tic douloureux. I feel it incumbent, however, to answer Dr. Strauss, certainly with reference to his suggestion that I operated on a potential and not an actual double tic. Let me assure you that such is not true. The patient had the double tic at the time of the operation; indeed she presented a very typical picture of double tic. This case was one of three recurrences that I had in the series. She had preservation of all sensory function in the face, and at least two thirds of the nerve had been divided. There are unquestionably, therefore, anatomic variations in the distribution of nerve tracts.

Dr. Cushing asks what would be the effect of dividing the anterior half of the sensory root. That I am unable to answer. I have not been willing to risk the possibility of failing to cure the pain when section of the posterior half of the sensory root has been so successful.

With reference to Dr. Hunt's question about the epicritic sensation, that has been tested and no change has been found. Dr. Howell has been very much interested in these observations because he thought that the neuron doctrine is at stake; I think he feels very much as I do about the results.

Dr. Strauss wondered if pain persists in the trigeminal area after section of the nerve. I know the type of pain that he means, the type of pain for which sympathectomy has been performed; I think that most — not all — pain of this kind is certainly of psychogenic origin. I have very carefully selected only those cases that are very typical ones of trigeminal neuralgia.

Dr. Harvey Cushing: Did Dr. Strauss not refer to the sensation of pain remaining present instead of to a spontaneous pain?

Dr. Israel Strauss: No, I referred to exactly what you referred to.

Dr. Dandy: One can differentiate sharpness and dulness and recognize painful impressions just as accurately as before, but the characteristic pain of tic douloureux is lost. There is, therefore, a difference in the type of pain.

I am unable to answer Dr. Elsberg's question. It may well be that his anatomic explanation has a bearing. I am unable also to say whether a division of the root at the gasserian ganglion is at all different from the division at the pons. One

would have to correlate the results secured by two different operators to determine this point. Unquestionably there is a rearrangement of the nerve fibers throughout the sensory root, i. e., between the ganglion and the pons. I think, too, that there are anastomoses between nerve fibers along the sensory root. Dr. Nouhuijs of Holland has studied the gross anatomy of the sensory root and has shown that many of the fibers on the anterior part of the ganglion pass immediately to the posterior part of the sensory root. These observations, he thought, explained the recurrences resulting from subtotal section of the sensory root at the ganglion as performed by Frazier.

Dr. Cushing asked whether the division of the optic nerve was homologous to the division of the sensory root of the fifth nerve. The only anatomic difference perhaps is that there may be an extra neuron in the optic nerve. It is a retroganglionic tract just as is the sensory root of the trigeminal nerve, the ganglion cells of course being in the retina. I think they probably are homologous.

INTRACEREBRAL VASCULAR NERVES *

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Unsolved problems in cerebral physiology and pathology demand an understanding of intracranial vascular changes. Until recently it has been taught that all intracranial vessels are devoid of vascular nerves and of vasomotor control, and that changes in blood flow through these vessels are produced only passively as a result of changes in systemic blood pressure. The physiologic [1] evidence (which will not be summarized here), however, has always been conflicting.

Anatomic evidence of vascular nerves on meningeal vessels has been steadily accumulating. After a preliminary negative report, Gulland [1a] described nerves on the blood vessels of the pia mater. Huber,[2] in an excellent piece of work, pointed out that there were nerves of two kinds on the pial vessels: (*a*) medullated fibers that terminated in nonmedullated branches, which he considered sensory, and (*b*) nonmedullated nerves, which he considered vasomotor.

Stöhr's [3] exhaustive studies of the vegetative nervous system demonstrated a rich plexus of nerves on arteries, and veins and capillaries in the pia and in the choroid plexuses of the ventricles. He described nerve endings of various types. Some of them were obviously sensory in form, and he [4] suggested that these might serve as the afferent portion of a circulation-regulating mechanism.

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* Submitted for publication, June 4, 1931.

* Read at the Fifty-Seventh Annual Meeting of the American Neurological Association, Boston, May 28, 1931.

1. The words "anatomic" and "physiologic" are used in order to conform with the terminology adopted by the ARCHIVES. The author would prefer to use the terms "physiological" and "anatomical."

1a. Gulland, L.: The Occurrence of Nerves on Intracranial Blood Vessels, Brit. M. J. **2**:781, 1898.

2. Huber, G. Carl: Observations on the Innervation of the Intracranial Vessels, J. Comp. Neurol. **9**:1, 1899.

3. Stöhr, P., Jr.: Mikroskopische Anatomie des vegetativen Nervensystems, Berlin, Julius Springer, 1928; Des peripherische Nervenfaser, in von Möllendorff: Handbuch der mikroskopischen Anatomie des Menschen, Berlin, Julius Springer, 1928, vol. 4, pt. 1, p. 143.

4. Stöhr, P., Jr.: The Nerves of the Blood Vessels, the Heart, Meninges, Digestive Tract and Urinary Bladder, in Cytology and Cellular Pathology of the Nervous System, New York, Paul B. Hoeber, Inc., 1931, vol. 1.

Huber, who used the intravital methylthionine chloride, U. S. P. (methylene blue) method, as well as Stöhr and Hassin,[5] both of whom used Schultze's modification of Cajal's reduced silver method, found that the nerve plexus of the pial vessels seemed to stop short when these vessels plunged downward into the brain or spinal cord. Stöhr showed me sections in which pial vessels turned at right angles and entered the brain. It was evident that the vascular nerves, which were clearly shown within the pia, either did not enter the brain with the vessel or else entered the brain with an altered staining reaction. That the latter alternative is actually true will be pointed out.

Hassin concluded that the inability to stain intracerebral vascular nerves meant that none existed, and suggested that the perivascular neuroglial footplates would leave no room for vascular nerves on the intracerebral capillaries. Nevertheless, Kölliker[6] had mentioned nerve fibers entering the brain on blood vessels of a diameter of 90 microns and less. This seems to have attracted little notice. Hunter[7] succeeded in staining a delicate plexus, which seemed to be nervous in nature, on the vessels of the cerebellum and brain stem of young rabbits, but he could not follow such a plexus into the white matter of the cerebrum.

Clarke,[8] in a careful piece of work in which he utilized Ranson's pyridine-silver method, demonstrated perivascular nerves in the medulla and spinal cord of cats and dogs, but failed to stain them elsewhere in the central nervous system. He reported two types of nerve fibers (as Huber had done in the pial vessels): (*a*) fine unmyelinated fibers that end in relation with the smooth muscle cells of the media, and (*b*) coarse fibers, possibly myelinated, that are continuations or collaterals of the myelinated fibers of the pial vessels and that end in the adventitia of the arteries. He found no nerves on intracerebral veins or capillaries.

Because of the insistent clinical and operative evidence that an intracerebral vascular reflex plays some rôle in the underlying mechanism of certain types of epilepsy (Foerster and Penfield,[9] 1930), I was led to

5. Hassin, G. B.: The Nerve Supply of the Cerebral Blood Vessels, in the Vegetative Nervous System, Baltimore, Williams & Wilkins Company, 1930, chap. 19, p. 437.

6. Kölliker: Handbuch der Gewebelehre des Menschen, Leipzig, W. Engelmann, 1893, vol. 11, p. 835.

7. Hunter, W.: On the Presence of Nerve Fibers in the Cerebral Vessels, J. Physiol. **26**:465, 1900.

8. Clarke, S.: Innervation of the Blood Vessels of the Medulla and Spinal Cord, J. Comp. Neurol. **48**:247, 1929.

9. Foerster, O., and Penfield, W.: Der Narbenzug am und im Gehirn bei traumatischer Epilepsie in seiner Bedeutung für das Zustandekommen der Anfälle und für die therapeutische Bekämpfung derselben, Ztschr. f. d. ges. Neurol. u. Psychiat. **125**:475, 1930.

undertake the study of the cerebral blood vessels. The problem, being initially a technical one, was begun by study of the vessels in normal subjects. I have now been able to demonstrate nerve fibers on the intracerebral blood vessels throughout the central nervous system by means of certain modifications in histologic method devised by our technician, E. Dockrill.

METHOD

The staining method used in the beginning was a modification of Cajal's reduced silver method, which gave good results in about one vessel out of fifty. This has been replaced by the Gros-Bielschowsky method, with the following modifications: To the formaldehyde fixative should be added any organic acid, preferably citric acid, to 10 per cent strength. Injection of the fixative should be made by the carotid if possible. The tissue should be left for two hours in the first silver nitrate solution. The best results are obtained after the tissue has been left for not longer than twenty-four hours in the fixative. This method has demonstrated vascular nerves on the intracerebral vessels of approximately 80 per cent of the cases in which it was used. The procedure has been progressively altered and improved up to the present, and may perhaps be further improved. All technical details will be published in the *American Journal of Pathology* when the evolution of the method ceases.

Use of the original methods without modification showed only pial vascular nerves. After the adoption of the modifications, vascular nerves in both places were demonstrated simultaneously. The material for study was obtained from the cat, dog, monkey (Macacus rhesus), chimpanzee and man. No morphologic differences were seen between these species.

Blood vessels were dissected from the brain as they pass into it through the pia. The vessel was kept under the focus of a binocular microscope, and brain tissue was pushed away from it with very fine metal spatulas. The vessel was then cut off with or without its pial attachment, carried through the staining process and mounted without being sectioned.

OBSERVATIONS

In the process of dissection, the vessels may sometimes be removed from the cerebral tissue in an easily separable sleeve, which is the inward continuation of the pia mater. In such a sleeve, veins, arteries and their branches for a short distance may be included (fig. 1). Delicate nerve fibers are found occasionally in the walls of this pial sleeve. These nerves may or may not show a connection with those on the adventitia of the vessels. A well developed pial sleeve is most easily demonstrated about the vessels that enter the brain directly from the middle cerebral artery and in the perforated spaces at the base of the brain.

Better staining of the perivascular nerves is obtained if this sheath is removed from the artery. Small arteries which under a coverslip measure from 40 to 60 microns in width and from 10 to 20 microns in depth may thus be excised and stained. Attached to such removed vessels will be found the smallest arterioles and capillaries.

The appearance of the vascular nerves is essentially the same in various areas of the cerebrum, the cerebellum, medulla oblongata and spinal cord. The nerve fibers are continuous with those of the pial vessels (fig. 2). They often pass irregularly around an artery or arteriole (fig. 3), giving off numerous collaterals and forming a loose net (fig. 4), or they may course like a long thread on the artery, gradually passing about it, but without branching. These fibers may lie

Fig. 1.—Drawing of an artery and vein entering the base of the brain accompanied by the invaginated pial sheath. This specimen was removed under the dissecting microscope from a normal human brain. The relationships that are indicated became evident when the tissue was dropped into Ringer's solution.

on or in the adventitia, but on the smaller arteries they run between the adventitia and the media.

The media of these small arteries is composed of an outer circular layer of smooth muscle and an inner longitudinal layer (figs. 5 and 6). The adventitia may be very thin, but the nerve fibers often lie distinctly beneath it. When the perivascular sheath is left intact about the artery,

nerves are sometimes seen to be present in this sheath. These nerves resemble those on the artery, and indeed sometimes definitely pass from the one to the other (fig. 6).

The great majority of the vascular nerve fibers are of very small caliber, being 0.5 micron or less in diameter, and presenting fusiform

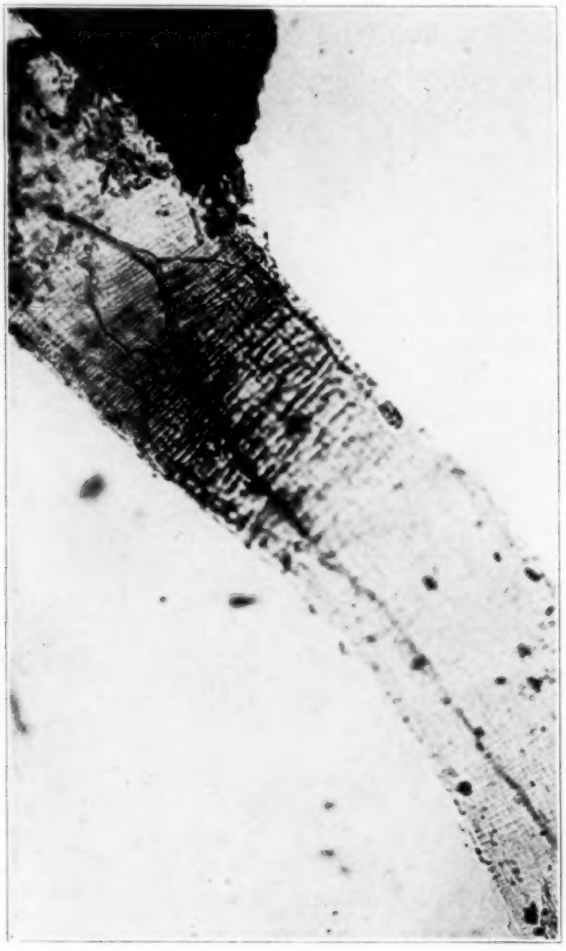

Fig. 2.—Vascular nerves are shown in the left upper corner leaving the pia and entering the brain on a deep cerebral vessel in the anterior perforated space of a cat; reduced from a magnification of 200.

enlargements. There are occasional coarse fibers the diameter of which is as much as 2.5 microns. In figure 7, a coarse and a fine vascular nerve may be seen keeping company on a small artery only 40 microns in width when flattened by the cover slip. These two types may well cor-

respond to the thick and thin fibers described by Huber (1899) in the pia mater. But the coarse fibers do not necessarily arise from myelinated pial nerves as was suggested by Clarke. This is shown by the fact that I have traced a nerve that was myelinated in the pia, but that lost its myelin sheath when it left the pia on an intracerebral vessel (fig. 8).

Fig. 3.—Vascular nerves encircling a small artery in the basal ganglia of a cat; × 340.

The nerve regained its myelin again for a short distance and then continued, a small fiber coated only with a nucleated sheath, but branching frequently (fig. 9). This nerve was not coarse, but fine and delicate. It is obvious therefore that nonmyelinated intracerebral nerves may be continuous with myelinated pial nerves, as well, no doubt, as with nonmyelinated ones. No ganglion cells have been seen on these vessels.

In general, the intracerebral vascular nerves seem to be altogether nonmyelinated and are covered by a nucleated sheath of Schwann. It must be admitted, however, that with silver stain it is impossible always to be sure that there is no myelin. The nucleated sheath may be seen easily at times as a sort of halo; at other times, it is slightly stained

Fig. 4.—Vascular nerves on a small artery in the frontal lobe of a cat. A thin sheath is stained about the nerve fiber. It is evident that the nerves are running just beneath the surface. Reduced from a magnification of 338.

(fig. 4), and at others no sheath is visible. The sheath of Schwann cells are likewise visible at times (fig. 10), and at other times invisible. Although the stain may show the nerve fibers clearly, other tissues have a variable affinity for the silver stains, as can be seen in the illustrations cited.

Fig. 5.—Drawing of an artery 10 by 70 microns entering the basal ganglia of a monkey. The nerve fibers are drawn as they appeared on all sides of the vessel, and therefore appear more numerous than in the photomicrograph. The nerves are situated directly on the outer surface of the muscularis. The relationship of the two layers of the muscularis is shown (*A* and *B*). Cells are seen coming down from the pia about the vessel, but the perivascular sheath is not indicated.

Fig. 6.—Vascular nerves on a small artery in the basal ganglia of a monkey. The perivascular sheath has been removed and clings to the artery. In order to complete the picture, the nerves, which were shown on a different level from that at which the photograph was taken, have been drawn in. The point at which the drawing was added to the one that has been photographed is indicated in each case by small arrows. The nuclei of the outer layer of the muscularis are stained and are in focus in some areas; × 203.

No nerve fibers have been seen on capillaries. This may be due to the method of removal. The nerves to the capillaries in the pia mater pass through the tissue from one to another (Stöhr).[10] It is difficult to conceive of a nerve with a sheath of Schwann passing through cerebral tissue. It would probably follow the arteriole to the capillary. At all events, I have seen no evidence of capillary innervation, but this does not mean that such innervation does not exist.

Fig. 7.—A coarse and a fine vascular nerve fiber on an artery in the basal ganglia of a cat; × 737. The width of the artery was 40 microns; its depth under the cover slip was about 10 microns.

The endings of intracerebral nerves are usually small grapelike or mushroom-like clusters, about 5 microns or less in diameter (fig. 11). Their size is in striking contrast to that of the ending on a pial vessel, which may be as large as 120 microns in diameter (fig. 12). The situa-

10. Stöhr (footnote 3, second reference).

Fig. 8.—Transition of a myelinated nerve fiber into a nonmyelinated fiber on a small artery just after it has left the pia to enter the brain. Anterior perforated space of a cat; reduced from a magnification of 1,100.

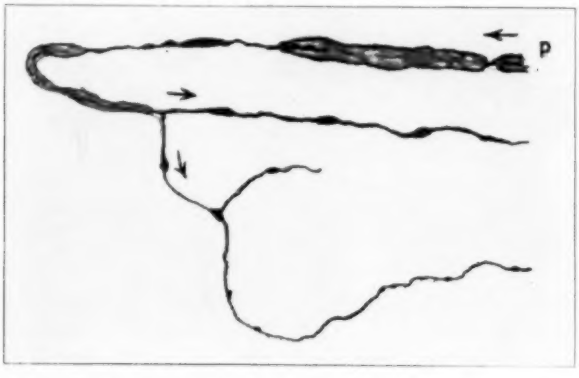

Fig. 9.—Drawing of the nerve that is shown in figure 8 to show the transition from a myelinated to a nonmyelinated fiber. *P* indicates the site of the pia. The nonmyelinated fibers were wrapped about the artery as it entered the brain.

tion of these intracerebral endings is beneath the adventitia and apparently in the media, although the exclusive specificity of the stain sometimes makes it difficult to determine the level of the ending.

In general, the intracerebral vascular nerves differ from the pial vascular nerves in that large myelinated nerve fibers ("trunk lines") are

Fig. 10.—Nerve fibers on a blood vessel in the frontal lobe of a monkey, showing the sheath of Schwann nuclei; × 900.

found only on the latter (fig. 13), and the large adventitial endings which resemble sensory terminations have not been found within the brain. The pial vessels do have an intimate reticulated plexus of nerve fibers that resembles the plexus on the intracerebral vessels, except that the former is more intricate and more frequently branching (compare figs. 4 and 14).

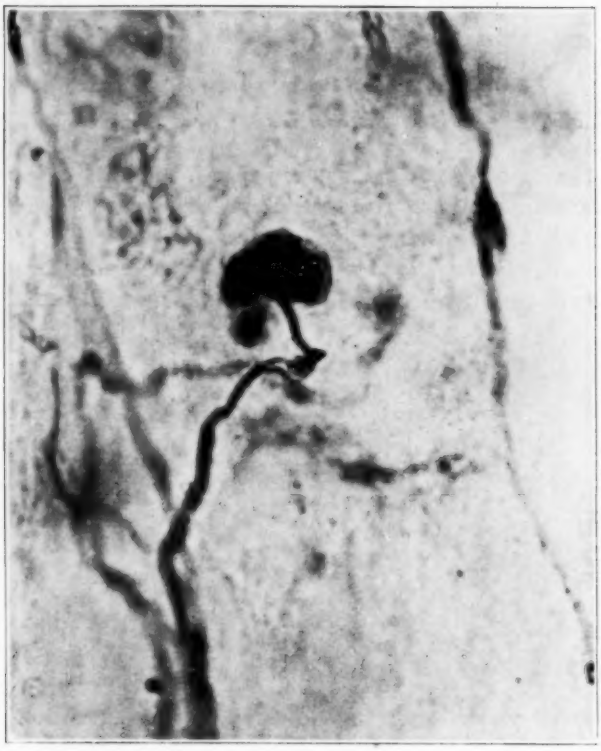

Fig. 11.—Nerve ending in the muscularis of an artery, 90 microns in diameter when flattened under the cover slip. Frontal lobe of a cat; × 3500.

Fig. 12.—Nerve ending, resembling a Meisner corpuscle, on the middle cerebral artery of a monkey. Only the wall of the artery is cut. Weigert-Pal stain; magnification × 156.

Fig. 13.—Myelinated nerves on the middle cerebral artery of a monkey. Weigert-Pal stain; magnification × 264.

Fig. 14.—Vascular plexus on the middle cerebral artery of a cat; magnification × 428.

The origin of these intracerebral vascular nerves forms the subject of an unfinished study. Sympathectomy in a large number of animals during the past two years indicates that the parentage of these nerves is not altogether in the sympathetic ganglia. The same conclusion in regard to the pial vascular nerves was reached tentatively by Huber (1899) after extended experimental work.

CONCLUSION

The intracerebral and intramedullary arteries (and to some extent the veins) are innervated in a manner similar to that of the blood vessels of the pia mater, and the two nerve plexuses are continuous. From a purely morphologic point of view, intracerebral vasomotor reflexes are possible.

OSTEITIS FIBROSA CYSTICA OF THE SKULL

ASSOCIATED WITH HEMIANOPIA AND PSYCHOTIC SYMPTOMS *

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AND
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DETROIT

Osteitis fibrosa cystica occurring as a solitary tumor of the skull is a relative rarity among diseases of the skeletal system. The association of such a lesion localized in the occipital bone with definite visual hallucinatory phenomena and an accompanying hemianopia, together with psychotic manifestations, is considered of sufficient importance to record in some detail. Of particular interest are the facts that the mental symptoms subsided to a noteworthy degree following an operation on the affected area and that the hallucinatory phenomena entirely disappeared.

Osteitis fibrosa cystica was called by Locke [1] a rare chronic degenerative disease of bone beginning in late childhood. He stated further that very rarely are cysts found in the skull. Bloodgood [2] specified two distinct types, the generalized or multiple cystic form and the localized or solitary cystic lesion. Their occurrence he believed to be rare before the age of 10 years or after the twentieth year. However, Frangenheim [3] considered the disease to be in existence long before its clinical recognition and found, in carefully traced histories, evidence of its existence before the tenth year. In a series of fifty cases published by Bloodgood [4] in 1920, there were none occurring in the skull.

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* Submitted for publication, April 6, 1931.

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1. Locke, E. A.: Osteitis Fibrosa Cystica, Oxford Medicine, New York, Oxford University Press, 1928, vol. 4, p. 445.

2. Bloodgood, J. C.: Benign Bone Cysts, Ostitis Fibrosa, Giant-Cell Sarcoma and Bone Aneurism of the Long Pipe Bones, Ann. Surg. **52**:145, 1910.

3. Frangenheim, quoted by Locke (footnote 1).

4. Bloodgood, J. C.: Bone Tumors, Benign Bone Cysts and Ostitis Fibrosa Cystica: Gross and Microscopic Features, South. M. J. **13**:888, 1920.

The etiology has long been a matter of controversy. Numerous theories have been advanced, but those of chief value attribute the process to trauma, infection or endocrine disorder. The traumatic theory would explain the production of the cystic areas on a basis of bone injury with bleeding, hematoma formation in the marrow cavity and resultant cystic degeneration. Schuster [5] cited a case of a large bone cyst occurring at the site of a trauma with the discovery of hemorrhage into the bone marrow. Von Recklinghausen,[6] whose description of the disease in 1891 affixed his name to the clinical syndrome, believed that trauma and other mechanical factors might produce the cysts and that the subsequent fibrosis and giant cell proliferation are but attempts at repair. Pommer [7] likewise believed that a hematoma of traumatic origin produced pressure atrophy which accounted for the cyst formation. In six cases reported by Sish,[8] trauma was definitely found to be the etiologic agent. In one of these cases there was involvement of the bones of the face, with pain and tenderness as the prominent symptoms.

Kästner [9] recently reported a case of osteitis fibrosa cystica of the humerus occurring at the site of repeated fractures. He attributed the development of the cyst to the trauma. In an attempt to harmonize the various theories as to etiology, Evans [10] proposed the classification of "osteitis fibrosa polycystica on a constitutional basis plus infection, osteitis fibrosa monocystica on an infectious basis plus trauma and a third diffuse type."

Mouchet and Le Gac [11] protested against trauma as the cause of the cystic tumors and cited the demonstration of well formed cysts two days after the occurrence of the trauma. Bolognesi,[12] after failing to produce bone cysts experimentally by trauma, refuted the theory of traumatic

5. Schuster, D.: The Origin of Bone Cysts, Beitr. z. klin. Chir. **123**:191, 1921; abstr., J. A. M. A. **77**:1292 (Oct. 15) 1921.

6. von Recklinghausen, F. D.: Die fibröse oder deformierende Ostitis, die Osteomalacie und die osteoplastische Carcinose in ihren gegenseitgen Beziehungen, Berlin, G. Reimer, 1891.

7. Pommer, G.: Zur Kenntnis der progressiven Hämatom- und Phlegmasieveränderungen der Rohrenknochen auf Grund der mikroskopischen Befunde im neuen Knochenzysten Fälle, Arch. f. Orthop. **17**:17, 1919-1920.

8. Sish, N.: Osteitis Fibrosa Cystica: Six Cases, Surg., Gynec. & Obst. **41**: 481, 1925.

9. Kästner, H.: Zur Ostitis fibrosa, Zentralbl. f. Chir. **56**:862, 1929; abstr., J. A. M. A. **93**:84 (July 6) 1929.

10. Evans, E. T.: Osteitis Fibrosa, Monocystica, Polycystica and Diffusa, Radiology **13**:530, 1929.

11. Mouchet, A., and Le Gac, P.: Cysts in the Bones, Arch. franco-belges de chir. **25**:337, 1922; abstr., J. A. M. A. **78**:1423 (May 6) 1922.

12. Bolognesi, J.: Ueber die Pathogenese der sogenannten Knochencysten, experimentelle Untersuchungen, Deutsche Ztschr. f. Chir. **131**:382, 1914.

origin. No doubt, in many cases an injury may call attention to a previously existing cyst, but an original remote and often seemingly insignificant trauma has been known to produce cysts that remained symptomless until a blow or even a sudden fracture called attention to the pathologic condition of the bone. Lotsch [13] likewise rejected the traumatic theory, as did also Phemister and Gorden.[14] The latter succeeded in isolating Streptococcus viridans from the cysts in two cases. They pointed to the clinically infectious course of the disease and emphasized the accompanying systemic reaction in support of the claim of an infectious etiology.

Localized cystic areas may be the precursors of generalized osteitis fibrosa cystica, and cases are on record to show the development of generalized skeletal involvement after the demonstration of a single cyst considered to be of purely circumscribed type. Bergman [15] stated that most of the so-called local types have areas elsewhere in the body, and he believed that the local areas seen in childhood may lead later to a generalized form of the disease. True, the generalized type must have some area of first appearance, but it is manifestly an error to consider the focal lesions purely the result of a generalized systemic disease. Error arises probably from the identical pathologic pictures presented by the localized and generalized types and the assumption that identical histologic pictures predicate an identical etiology.

Da Costa,[16] in 1915, believed that the malacias were due to the absence or perversion of some internal secretion, possibly that of the parathyroid glands. Erdheim's [17] discovery of parathyroid hypertrophy in cases of osteomalacia led to vigorous investigation of the endocrine system. He attributed this hypertrophy to a compensatory effort on the part of the parathyroid glands to maintain the calcium balance, which is often seriously altered in the malacias. Mandl,[18] in 1925, acting on Erdheim's implication, successfully engrafted normal human parathyroid glands in a patient with osteitis fibrosa cystica. The patient became worse. Mandl then investigated the parathyroid glands by sur-

13. Lotsch, F.: Ueber generalizierte Ostitis fibrosa mit Tumoren und Cysten zugleich ein experimenteller Beitrag zur Aetologie der Knochencysten, Arch. f. klin. Chir. **107**:1, 1915.

14. Phemister, D. B., and Gordon, J. E.: The Etiology of Solitary Bone Cyst, J. A. M. A. **87**:1429 (Oct. 30) 1926.

15. Bergman, Ernst: Von der lokalisierten zur generalisierten Ostitis fibrosa, Arch. f. klin. Chir. **141**:673, 1926.

16. Da Costa, J. C., quoting Higbee and Ellis, in Modern Surgery, ed. 7, Philadelphia, W. B. Saunders Company, 1915.

17. Erdheim, J., quoted by Wilder, R. M.: Endocrinology **13**:231, 1929.

18. Mandl, F.: Therapeutischer Versuch bei einem Fall von Ostitis fibrosa generalisata mittels Exstirpation eines Epithelelkörperchentumors, Zentralbl. f Chir. **53**:260, 1926.

gical exposure and found adenomatous tumors. He concluded that this hypertrophy was the cause rather than the result of the bone disease. Wilder [19] reported a case of tumor of a parathyroid gland with hyperparathyroidism associated with osteitis fibrosa and classified the syndrome as a clinical entity — the antithesis of tetany. Barr and Bulger [20] reviewed the subject and are in agreement with Wilder. Hannon and his associates,[21] in a minute study of a patient with osteitis fibrosa cystica, concluded that hyperparathyroidism was the cause of the skeletal disease. The syndrome has been found when but one of the parathyroid glands was involved. Such was the observation of Compere,[22] who removed one pair of the glands and found an adenoma in one gland while the other was of normal structure. Mandl,[23] in 1926, sharply separated the two types of osteitis fibrosa cystica, regarding the generalized form as due to disturbances of the endocrine system, particularly of the parathyroid bodies, and the localized form as due to the action of trauma. The parathyroid glands are not exclusively affected, and instances of pituitary dysfunction have been reported. Heard, Schumacher and Gordon [24] stressed the relation between diabetes insipidus and osteitis fibrosa cystica. Abraham [25] has recently reported a case of diabetes insipidus associated with the polycystic form of osteitis fibrosa, with a large destructive lesion of the frontal bone. It is generally accepted that parathyroid hypertrophy (hyperactivity) produces a hypercalcemia by the extraction of calcium from bone. The excess calcium in the serum is then deposited in other organs of the body or is excreted.

Involvement of the nervous system has been reported but rarely as a complication of osteitis fibrosa. Nonne [26] cited four cases with symptoms referable to the nervous system, and he stated that often in obscure

19. Wilder, R. M.: Hyperparathyroidism: Tumor of the Parathyroid Glands Associated with Osteitis Fibrosa, Endocrinology **13**:231, 1929.

20. Barr, D. P., and Bulger, H. A.: The Clinical Syndrome of Hyperparathyroidism, Am. J. M. Sc. **191**:449, 1930.

21. Hannon, R. R.; Shorr, E.; McClellan, W. S., and DuBois, E. F.: Osteitis Fibrosa Cystica (Osteomalacia?) with Evidence of Hypertrophy of the Parathyroid Bodies, J. Clin. Investigation **8**:215, 1930.

22. Compere, E. L.: Bone Changes in Hyperparathyroidism, Surg., Gynec. & Obst. **50**:783, 1930.

23. Mandl, F.: Klinisches und experimentelles zur Frage der lokalisierten und generalisierten Ostitis fibrosa, Arch. f. klin. Chir. **143**:1, 1926.

24. Heard, J. J.; Schumacher, F. L., and Gordon, W. B.: The Association of Diabetes Insipidus with Osteitis Fibrosa Polycystica, Am. J. M. Sc. **171**:38, 1926.

25. Abraham, S.: Diabetes Insipidus and Osteitis Fibrosa Polycystica, J. A. M. A. **95**:483 (Aug. 16) 1930.

26. Nonne, M.: Die Ostitis fibrosa in ihren neurologischen Beziehungen, Deutsche Ztschr. f. Nervenh. **105**:35, 1928.

cases the only discernible symptoms are of neurologic origin. Headaches, neuralgias, epileptiform seizures and visual disturbances are among the most severe of the neurologic manifestations. Ehrlich [27] reported a case of osteitis fibrosa cystica with a variety of psychic symptoms and extensive involvement of the nervous system. Because of the patient's history of frontal presentation at birth and proof of the existence of the disease in childhood, Ehrlich was tempted to attribute the etiology to trauma sustained at birth.

REPORT OF CASE

History.—A girl, aged 14, of Russian Jewish parentage, was admitted to the Pennsylvania Hospital, department for mental and nervous diseases, on Jan. 2, 1930. Her complaints were dizziness, numbness and weakness of the extremities, a sense of pressure in the head and visual and auditory hallucinations. The father was of foreign birth, the son of a rabbi. He was 40 years of age and suffered from fibrotic pulmonary tuberculosis. There was evidence of severe gastric neurosis in his make-up. He was considered effeminate and inadequate, and was described as sensitive, high-strung, surly, overly jealous and dependent on his wife for the management of the household. The patient reacted negatively toward the father and felt that he had rejected her in favor of the other children. The mother, aged 38, was highly neurotic and unstable. She was, nevertheless, the commanding figure in the household. She had had several "nervous breakdowns," and had a cardiac lesion, which added to her instability. The patient reacted to her with excessively professed love, and many of her guilt feelings originated from the mother's neurotic episodes. The remainder of the family history was without significance, except that a diagnosis of psychopathic personality had been rendered in the case of a maternal aunt. The other siblings, aged 10 and 5, were normal except for neurotic tendencies.

The patient was born on May 19, 1915, after a normal, full term pregnancy. She was a fat, chubby baby; she was breast-fed, and was weaned at 9 months. Walking, talking and dentition occurred at normal ages. On July 24, 1917, at the age of 26 months, the patient fell down a flight of steps and sustained an injury to the skull. She was taken to a hospital, where a roentgen examination revealed a fracture of the occipital bone. She was unconscious for about twenty-four hours, but there were no evidences of cerebral injury. She was discharged on the sixth day, apparently in a good condition. The subsequent medical history was not significant except for the onset of menses at the age of 12.

Personality.—Up to the age of 9 years, the patient was normal in all her interests and activities; no eccentric trends were noted. At this age, however, she changed noticeably, becoming seclusive, quiet and dependent, and she showed a decided lack of initiative. She gradually became complaining, domineering and nagging. She had no interest in playing with other children unless she could dominate the field, direct the proceedings or reign as a queen commanding others to do her bidding. Jealousy and antagonism were manifested toward her brother and sister, and she complained of being neglected by her parents and of favoritism shown to the other children. Because of a long cherished ambition to become a teacher, she continued her school work, but after three years her interest lagged and she cared for little

27. Ehrlich: Umschiebene Ostitis fibrosa des Schadels, Fortschr. a. d. Geb. d. Röntgenstrahlen **38**:652, 1928.

except stories and newspaper accounts of suicides and murder. The games of the other children annoyed her, and she drove them from her vicinity. About this time she felt that her school mates were making fun of her and laughing at her plump, squat figure.

Present Illness.—At the age of 12, the patient's complaints had become intensified. Symptoms described as "aching and sticking pains" in her head were present, and she had to be removed from school because of fits of weeping and screaming. She was "jumpy" and felt that people were staring at her. The mother was unable to cope with the problem and had to leave the home because of an impending nervous breakdown. The patient developed pronounced feelings of guilt, believing that she was the cause of her mother's neurosis. Fears became manifest. Dream states occurred which were described by the patient as "faint-like feelings." Fears overwhelmed her, and she became apprehensive. In April, 1929, the dream states, periods of abstraction, "faint-like feelings" and transitory amnesias became more frequent and more profound. She seemed confused. Sex conflicts arose, and she performed masturbation as many as ten times daily. The act was accomplished by manipulation of the genitals through several layers of toilet paper or by titillation of the clitoris. This further added to her feelings of guilt. In May, 1929, she called her parents' attention to a "soft spot" in the occipital region, but they gave little credence to the complaint. The pain was localized over the occipital bone in the region of the skull defect, but often occurred as a severe generalized headache. She gradually became depressed, talked a great deal of suicide, cried frequently and complained of hearing voices. The voices were heard during the spells of abstraction, and she was unable to relate what they said. Visual hallucinations also occurred during this time, but were crude flashes of light or shapeless dark objects. She was taken to a physician, who advised the parents to ignore her complaints and return her to school. After an attempt at suicide by drinking tincture of iodine, she was taken to the Institute for Child Guidance, in New York, where Dr. L. A. Schwartz established the genuineness of her complaints and sent her to this institution.

Physical Examination.—The patient's height was 56.9 inches (142.25 cm.), or 9 per cent below the average for her age. Her weight was 120 pounds (54.4 Kg.), or 32 per cent above the average for her age. She was a precociously developed Jewish girl who looked older than her stated age. The striking feature of the physical study was the bony defect in the skull. This was an area extending from the external occipital protuberance to the upper border of the occipital bone, about 4 cm. in width and 9 cm. in length. The external bony wall was thin, and craniotabes was elicited on digital pressure over the area. The patient evinced pain which radiated to the right mastoid region, and she claimed to hear a crackling noise when pressure was applied. The neck was short and full, and the thyroid gland was palpable. There was no palpable tumor in the regions of the parathyroid glands. The breasts were large and pendulous, and decidedly abnormal for the patient's age. The blood pressure was 120 systolic and 88 diastolic. The abdomen was fat and soft. There was a thick mat of black pubic hair, showing a normal feminine distribution, which was definitely precocious for a girl aged 14. The hips were wide and full, and the lower extremities were short and chubby. The arms were short, and the hands were wide and stubby with fat bulbous thumbs.

Mental Examination.—The patient, throughout the psychiatric examination, gave an impression of apathy and depression. She preferred idleness and day dreaming to activity of any kind. There were momentary escapes from reality, abstractions, periods of preoccupation, amnesias and dream states or "faint-like feelings" of increasing frequency. There was at times a tic of the left facial muscles associated

with an involuntary spasm of the upper half of the left side of the face. During most of our interviews, she sat gingerly on the edge of her chair with a staring immobile expression. The train of thought was retarded and constantly interfered with by fantasies. After arousing her interest, there was some degree of continuity in her discourse. Her dominant mood was one of depression, though at times she broke into apparently unmotivated laughter. She wanted to die, and suicide fantasies occupied her mind. Her trend revolved about her illness. Delusions, ideas of reference, feelings of frustration and futility were prominent. The hallucinations were of a crude nature; the visual impressions were usually experienced as vague sensations of light, occasionally as bright clusters and again as glowing shapeless objects. On closing her eyes, she saw dark shapeless objects moving about. The auditory hallucinations were likewise indefinite. She stated that they occurred as "words crossing her mind," but the words were as if spoken to her. She was able to repeat only two of the curious phrases, namely, "death" and "lungs over."

Neurologic Examination.—In addition to the previously mentioned evidences of hypothyroidism and hypopituitarism, there was a marked general weakness and

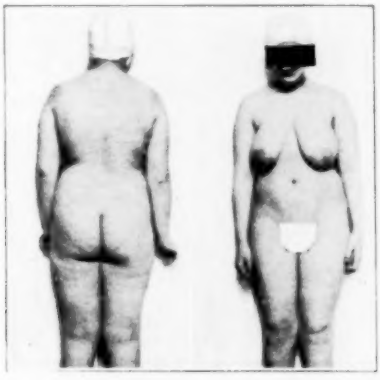

Fig. 1.—Frontal and dorsal views of the 14 year old patient, showing the tremendous mammary hypertrophy and the body contour and stature suggestive of endocrine dysfunction.

feeling of profound fatigue. The hand grips were less than 5 on the dynamometer, and the gait was slow and cautious. Swaying was present in the Romberg position. A twitching of the muscles of the right arm was occasionally noted, and subjectively the patient complained of numbness over the shoulder and forearm. The tendon reflexes were uniformly hyperactive. There was a slight impairment of hearing in the left ear. An examination of the eyegrounds revealed normal fundi. The patient was transferred to the University of Pennsylvania Hospital, to the neurologic service of Dr. William G. Spiller. The visual fields, recorded by Dr. Wentworth, disclosed left homonymous scotomas with an enlarged blindspot on the right and including the blindspot on the left. The visual field defects were interpreted by Dr. Spiller as indicating a bilateral lesion of the papillomacular bundle, due probably to compression of the calcarine cortex of the right occipital pole by the intruding inner wall of the bone tumor.

Laboratory Examinations.—Examination of the blood showed: red cells, 4,800,000; hemoglobin, 93 per cent; white cells, 12,800, with a differential count of

66 per cent polymorphonuclears, 30 per cent lymphocytes, 3 per cent monocytes and transitional cells, and 1 per cent eosinophils. All urinalyses gave normal results. The Wassermann and Kahn reactions of the blood were negative. Chemical analysis of the blood showed: urea nitrogen, 8.5 mg.; blood sugar, 100 mg.; calcium, 8.8 mg., and phosphorus, 4.4 mg. per hundred cubic centimeters. The spinal fluid was under a pressure of 12.5 mm. of mercury, contained 3 lymphocytes per cubic millimeter and showed an absence of globulin and a colloidal gold curve of 0000000000; the Wassermann reaction was negative. The basal metabolic rate was —28 per cent, and on subsequent tests —27 and —18 per cent.

Roentgenologic Examinations.—Dr. H. K. Pancoast reported: "There is a large cranial defect involving the occipital bone, extending from the lambdoid suture to the rim of the foramen magnum. The tangential view shows a thin shell of bone posteriorly, representing what remains of the outer table. We are unable to dem-

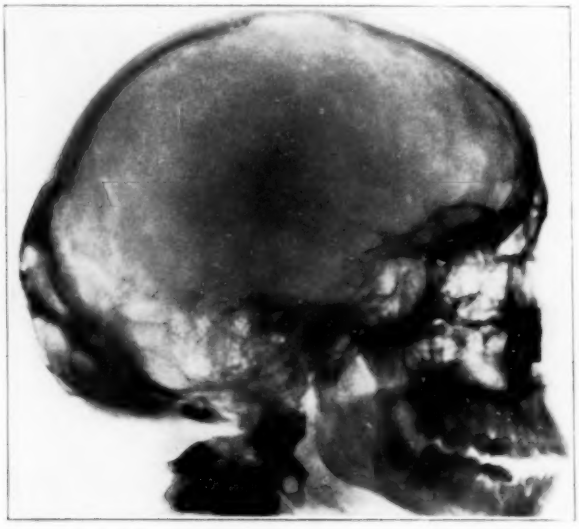

Fig. 2.—Tangential view of the skull, showing the cystic lesion in the occipital bone and the intrusion of the inner wall of the cyst into the cranial cavity. The paper thinness of the external bony wall is evident.

onstrate the outline of the inner table. The diagnostic possibilities are: (1) osteitis fibrosa cystica; (2) xanthomatosis; (3) chloroma; (4) congenital syphilis; (5) cholesteatoma. We believe that the lesion represents the terminal stage of osteitis fibrosa cystica, especially in view of the history of fracture of the base of the skull twelve years ago."

Operation.—A craniotomy was performed by Dr. Charles H. Frazier in the right occipital region on April 25, 1930. Colonic anesthesia, supplemented by inhalation of ether at the end, was employed. Dr. Frazier noted: "An osteoplastic flap was directed temporalward sufficient to uncover all of the right occipital lobe, disclosing the dura beneath. Along the median side of the circular opening in the bone could be seen a large swelling in the diploe, about 2.5 cm. thick at the center (maximum), which projected inward and tended to compress the brain beneath it. The swelling (tumor of bone) was punctured and found to be a hollow

cyst. The bulging inner wall of this bony cyst was resected with rongeur forceps, leaving a dead space between the brain and the outer cyst wall (the cranium). This space was approximately 7 x 5.5 x 2.5 cm.

"The dura and the pia were torn slightly at a point beneath the cyst where there were present some thickening and adhesion of the dura to the cyst wall. This rent was sutured. A longitudinal incision in the dura the full length of the flap opening was made as an exploratory measure which revealed no pathologic condition beneath. This was closed with interrupted silk sutures.

"The inner side of the bone flap was treated for hemostasis by impregnating paraffin wax in the dead spaces and further by coagulating high frequency current applied to the bleeding points. The osteoplastic flap was then replaced and sutured to the scalp by two rows of interrupted silk sutures."

Postoperative Record.—The immediate postoperative results were satisfactory, but infection developed in the wound and for a considerable time two sinuses existed

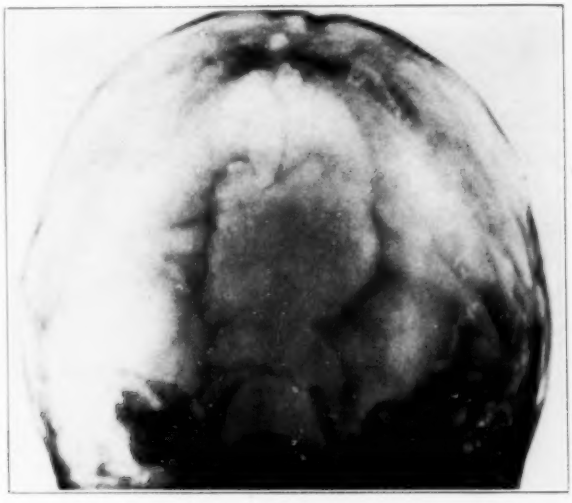

Fig. 3.—Anteroposterior view, showing the large bone defect, occupying the full length of the occipital bone from the foramen magnum to the lambdoid suture. The defect is at the site of the trauma sustained twelve years before the onset of symptoms.

which discharged a considerable amount of pus. The patient was observed for eleven weeks after the operation. She gained strength slowly, but before discharge from the hospital she was able to enter into all forms of recreation. Mentally, there was a striking change; the degree of improvement can probably be best judged by two letters written to her family.

On June 5, 1930, five weeks after the operation: "My dear family, I am so happy I could sing and dance but I am not quite strong enough to dance yet. Isn't it swell to want to live? It seems I woke up all of a sudden in a new world. I don't even remember how I was before. Aren't you glad everybody that I am better?"

On June 8, 1930: "My dear mother and father, Dear Mamma, I am so much better. Everything is gone except the pain. Isn't that great? I don't want to

die now, I want to live and I'm only dreaming of the time I'll come home and you will be making me well and strong again. It's all over now except the pain."

The hallucinations had disappeared after the first week, and there had been no recurrence at the time of discharge on July 15, 1930. Aside from some irritability and peevishness at her weakness, she was entirely normal in all reactions. She showed clear insight into the hallucinatory episodes, and before discharge she entered into all recreational activities, adjusting herself socially in a satisfactory manner.

Summary.—On July 24, 1917, the patient, then 26 months of age, sustained a fracture of the occipital bone, as demonstrated by roentgenograms, and after a brief period of unconsciousness seemed normal. At the age of 9, a change of personality occurred which by the age of 12 had assumed psychotic proportions. A bone defect was noted in the occipital

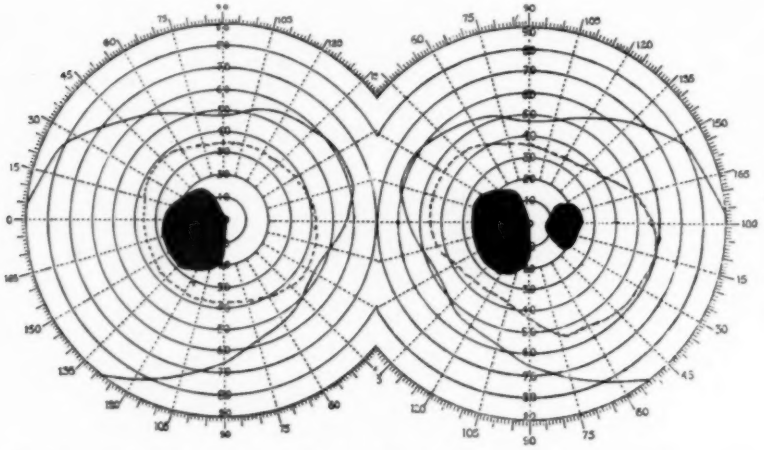

Fig. 4.—Visual fields, showing the left homonymous scotomas, including the blindspot on the left, and with an enlarged blindspot on the right.

region at the age of 12 and was confirmed by a roentgenologic study two years later. The lesion was diagnosed as localized osteitis fibrosa cystica. The mental symptoms became so pronounced that confinement in a psychiatric institution was necessary. Predominating symptoms were headache, apathy, depression, a sense of unreality, dream states, and periods of amnesia and abstraction of varying duration, during which the patient heard voices and experienced visual hallucinations of a vague nature. The patient recognized these abnormal phenomena and showed insight into her condition. The mood was one of depression and anxiety; there was a pronounced suicidal trend, and a history of attempts by poison. Neurologic examination showed the presence of left homonymous scotomas which suggested a bilateral lesion of the macular bundle pointing to a focal lesion at the calcarine cortex of the right occipital

pole. Pressure of this bone cyst was believed to be the cause of origin of the hallucinatory phenomena and the homonymous scotomas. A right occipital craniotomy was performed, and the protruding inner wall of the large cyst rongeured away. Postoperative observations showed a pronounced change in mood with a complete disappearance of the hallucinations and subsidence of the mental symptoms.

COMMENT

Hallucinations associated with organic lesions of the brain have been reported in the literature. Westphal,[28] in 1879, wrote of hallucinatory episodes in a patient who at necropsy showed atrophy and softening of the posterior half of the right hemisphere. Seven years later, Seguin [29] commented on hallucinatory images seen in the blind portion of the hemianopic visual field, and stated his belief that such phenomena represented an irritation of the cortical visual center just previous to destruction. A certain psychopathologic interpretation of such hallucinations is necessarily interjected, but some writers, notably Hughlings Jackson, believed that hallucinations might be provoked as distant effects of tumors by irritation of higher mental centers rather than by the effect of a focal irritative lesion. It was not possible in the case here reported to localize the visual images in the hemianopic area, though the images were of the crude nature described by Horrax [30] as occurring in the blind portion of the hemianopic visual field in cases of tumors in the occipital lobe. Horrax differentiated two types of hallucinations, those arising from lesions of the temporal lobe being of the elaborate, more highly differentiated type, and those arising from lesions of the occipital lobe being of a crude, undifferentiated character. Yandelson [31] has said that hallucinations of sight point definitely to a localization in the occipital cortex.

The incomplete homonymous hemianopia is remarkably similar to that in a case quoted by Scarlett and Ingham.[32] Their patient showed visual field defects, identical with those of our patient, due to a wound (bullet) in the right occipital lobe.

28. Westphal, C.: Zur Frage von der Lokalisation der unilaterale Convulsionen und Hemianopsie bedingenden Hirnerkrankungen, Charité-Ann. **6**:342, 1879.

29. Seguin, E. C.: A Contribution to the Pathology of Hemianopsia of Central Origin (Cortex-Hemianopsia), J. Nerv. & Ment. Dis. **13**:1, 1886.

30. Horrax, G.: Visual Hallucinations as a Cerebral Localizing Phenomenon, Arch. Neurol. & Psychiat. **10**:532 (Nov.) 1923.

31. Yandelson, A.: Mental Conditions Associated with Disease of the Brain and Cranial Nerves of Special Sense, Illinois M. J. **46**:268, 1924.

32. Scarlett, H. W., and Ingham, S. D.: Visual Defects Caused by Occipital Lobe Lesions, Arch. Neurol. & Psychiat. **8**:225 (Sept.) 1922.

Psychotic reactions were studied in a group of forty-six cases of tumor of the brain by Morse,[33] who found a constant series of symptoms, chiefly impairment of memory, amnesias, emotional changes and hallucinations. One of her cases, that of a patient with a cholesteatoma encroaching on the left hemisphere, bears a striking resemblance to the case reported here. The symptoms of headache, slight fainting attacks, periods of drowsiness and numbness in the extremities were remarkably similar to the complaints of our patient. Cushing [34] has called attention to the sense of unreality, dream states, petit mal phases and visual and auditory hallucinations in certain tumors of the temporal lobe. Allen [35] recently studied the clinical features in forty cases of tumor of the occipital lobe and mentioned visual hallucinations as occurring in 25 per cent, auditory hallucinations in 5 per cent, headache in 95 per cent, spontaneous subjective sensations in 30 per cent, mental changes in 60 per cent and contralateral homonymous defects in the visual fields in 94 per cent. Strecker and Ebaugh [36] found some rather striking personality disorders attributable to diffuse cerebral injury resulting from trauma. Taft and Strecker [37] reported a case of a frank psychosis that lasted three decades and was associated with a small dural tumor determined by a remote trauma. Hallucinatory episodes occurred in their patient, but were not constant or well defined. Yandelson [31] believed that psychotic reactions in cases of tumor of the brain are due to a cellular disarrangement caused by the encroachment of the neoplasm. He cited apprehension, affective disturbances and amnesia as predominating psychic symptoms in cerebral tumor.

SUMMARY

The case reported is one of localized osteitis fibrosa cystica resulting from an injury to the skull in infancy and giving rise to neurologic symptoms twelve years after the occurrence of the trauma. The etiologic rôle of the trauma is significant since recent literature has tended to designate the generalized form as dependent on parathyroid hyperplasia and the local type as determined purely by trauma. Yet it is obviously very rare that bone injury alone leads to the formation of cystic areas

33. Morse, M. E.: Brain Tumors as Seen in Hospitals for the Insane, Arch. Neurol. & Psychiat. **3**:417 (April) 1920.

34. Cushing, H.: Distortions of the Visual Fields in Cases of Brain Tumor: VI. The Field Defects Produced by Temporal Lobe Lesions, Brain **44**:341, 1921.

35. Allen, I. M.: A Study of Tumors Involving the Occipital Lobe, Brain **53**:194 (July) 1930.

36. Strecker, E. A., and Ebaugh, F. G.: Neuropsychiatric Sequelae of Cerebral Trauma in Children, Arch. Neurol. & Psychiat. **12**:443 (Oct.) 1924.

37. Taft, A. E., and Strecker, E. A.: Psychosis Associated with Trauma of the Head, Arch. Neurol. & Psychiat. **14**:658 (Nov.) 1925.

of osteitis. In the light of recently established relationship between endocrine imbalance and the malacias, it may be conjectured that there are conditioning endocrine factors in patients who develop cystic bone lesions following a trauma, resulting in a disordered metabolism and predisposing to anomalous repair with typical cyst formation.

Focal compression of the right occipital pole by the intrusion of the inner wall of the bone cyst produced a lesion of the calcarine cortex, evidenced by the incomplete left homonymous hemianopia. Irritation of the visual cortex in this area occasioned visual hallucinatory phenomena. The similarity between the picture presented by our patient and that of patients with tumors of the occipital lobe is worthy of emphasis. The differential diagnosis rested largely on the roentgenologic observations.

The picture was complicated and somewhat overshadowed by the psychotic symptoms. These were regarded as remote or indirect manifestations of the organic lesions. A psychopathologic basis of the patient's reactions must be evaluated, especially when viewed in relationship to the personality as a whole. The precocious sexual development and the structural peculiarities of the patient are factors that may have produced inferiority feelings and forced compensations of an eccentric nature, leading ultimately to withdrawal from reality, intense autoerotism and other regressive trends. A psychoanalytic interpretation is intriguing, but elaboration of the more deeply lying psychic mechanisms is deemed unwarranted in this presentation.

PERIPHERAL NERVES

ANATOMIC AND PATHOLOGIC CONSIDERATIONS *

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In studying normal or pathologic peripheral nerves, one is confronted with a number of uncertainties, if not riddles, pertaining to both their normal and their pathologic histology. For instance, no definite information is available as to what actually makes up a normal peripheral nerve or how to interpret some phenomena occurring in such common conditions as peripheral nerve degeneration or regeneration. A discussion of some such problems is the object of this contribution. The observations here recorded have been made on the instructive material placed at my disposal by Spielmeyer (Munich), Nageotte (Paris) and Ranson (Chicago), but these gentlemen, of course, are not responsible for the views here advocated. The human material of Professor Spielmeyer—180 war cases, only a part of which I studied—was, like the rich experimental material of Nageotte and Ranson, ready for microscopic study. Though there are some disadvantages in using ready material, since additional, especially staining, methods of study cannot be employed, there is the great advantage of saving considerable time when abroad.

While the anatomy of the peripheral, in contrast to that of the central, nervous system is admittedly less complicated, the structure of a peripheral nerve fiber is decidedly much more complex than that of a central nerve fiber. The axon, myelin, Schwann cells, Schwann sheath and mesodermal membranes are only the essential and probably the best studied, but by no means the only, constituents of a peripheral nerve fiber. The axon, for instance, which is present in every nerve fiber, is made up of neurofibrils, each neurofibril being surrounded by an amorphous substance (axoplasm). According to some investigators,[1] the axonal neurofibrils form anastomoses, the existence of which is denied by the latest investigators, among them de Rényi.[2] The axon

* Submitted for publication, March 25, 1931.

* Presented at a Joint Meeting of the New York Neurological Society and the Section of Neurology and Psychiatry of the New York Academy of Medicine, March 10, 1931.

1. Walter, F.: Zur Kenntnis der peripheren markhaltigen Nervenfasern, Deutsche Ztschr. f. Nervenh. **35**:152, 1908.

2. de Rényi, George S.: Observations of Neurofibrils in the Living Nervous Tissue of the Lobster, J. Comp. Neurol. **48**:441, 1929.

is supposed to possess a membrane of Mauthner or an inner Schwann sheath which, enveloping the myelin, separates it from the axon. The existence of either is generally denied. Nemiloff,[3] for instance, maintained that only a coagulated substance exists between the axon and myelin, while Nageotte[4] spoke of an actual space between the axon and myelin filled with a fluid emanating from the former. By injecting the nerve fibers, de Rényi was able to demonstrate a connection between the axon and myelin and the existence of a narrow cavity which he could enlarge by "continuing the injections."

Of a more complicated structure is the myelin. When fresh and properly fixed, it is homogeneous and smooth, and shows a number of structures. Of these I shall mention the best known: the incisures of Schmidt-Lantermann, with annular rings and spirals of Rezzonico-Golgi; the nodes of Ranvier; the double spinous bracelets of Nageotte, and the neurokeratin network of Ewald and Kühne (fig. 1). The latter does not yield to the action of digestive ferments (trypsin), ether, alcohol or chloroform. Like the incisures of Schmidt-Lantermann and their contents—Rezzonico-Golgi spirals—the neurokeratin is considered, probably unjustly, to be an artefact. At any rate, the structures mentioned still are objects of controversy. Cajal considered them real formations, mechanical supporters of the myelin, the rings maintaining the cylindric form of the nerve fibers. As to the nodes of Ranvier, these are recognized universally as preexisting formations, while the existence of the double spinous bracelets of Nageotte has been of late confirmed by de Rényi.[5] After injecting the nerve fibers, he found that at the nodes of Ranvier the axon is much closer to the myelin than elsewhere, thus denoting the presence there of a substance holding the stump of the myelin very firmly to the axon.

As to the network repeatedly described in the myelin, Nemiloff,[3] Doinikow[6] and Edinger[7] maintained that the latter is enclosed within a net of fibers emanating from the cells of Schwann. The long proc-

3. Nemiloff, A.: Einige Beobachtungen über den Bau des Nervengewebes bei Ganoiden und Knochenfischen, Arch. f. mikr. Anat. **72**:575, 1908; **79**:639, 1912.

4. Nageotte: L'organisation de la matière dans ses rapports avec la vie, Paris, Félix Alcan, 1922, p. 268.

5. de Rényi, George S.: The Structure of Cells in Tissues as Revealed by Microdissection, J. Comp. Neurol. **48**:293, 1929.

6. Doinikow, B.: Zur Histopathologie der Neuritis mit besonderer Berücksichtigung der Regenerationsvorgänge, Deutsche Ztschr. f. Nervenh. **46**:20, 1912; Beiträge zur Histopathologie des peripheren Nerven, in Nissl and Alzheimer: Histologische und histopathologische Arbeiten über die Grosshirnrinde, Jena, Gustav Fischer, 1911, vol. 4, p. 487.

7. Edinger, L.: Untersuchungen über die Neubildung des durchtrennten Nerven, Deutsche Ztschr. f. Nervenh. **58**:1, 1918.

esses of the latter, branching from the perinuclear cytoplasm, extend over the myelin, which they not only envelop but actually invade down to the axon. A connection is thus established between the axon and myelin which is not broken up by the invading processes of Schwann cells, but is continuous through the spongy mass formed by them. According to such a conception, the myelin is a mere enclosure of the Schwann cell and its branches, the ramifications of which within the myelin are supposed to represent the much discussed net of neurokeratin. Attractive and plausible as such views may be, they were not confirmed. Neurokeratin meshes, however, undoubtedly exist, being,

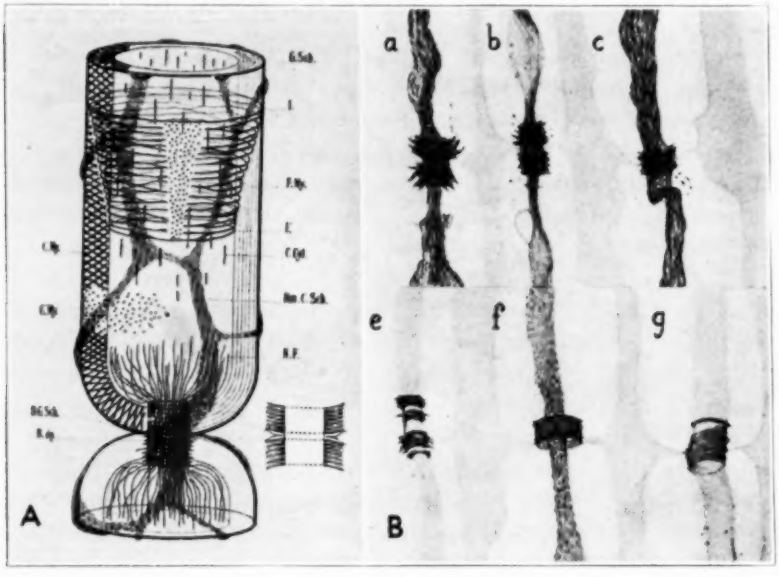

Fig. 1.—*A* is a diagram by Nageotte, showing some of the structures of a peripheral nerve fiber. To the right in *A* is a longitudinal section of a node. *F.My.* indicates myelin and its lamellae; *C.My.*, mitochondriae of the myelin sheath; *C¹My.*, as they appear over the "surface of the myelin"; *B.ep.*, double bracelets; the lower shows the spines; *C.Cyl.*, mitochondriae of the axis cylinder; *I.* and *I¹.*, Schmidt-Lantermann's incisures containing the apparatus of Rezzonico and granules; *G.Sch.*, Schwann membrane; *D.G.Sch.*, diaphragm of Schwann's membrane; *Rm.C.Sch.*, protoplasmatic marginal net of a Schwann cell; *N.F.*, neurofibrils. *B* shows a variety of Nageotte's double spinous bracelets from the cauda equina of a guinea-pig; at *f*, only one half of the bracelet is stained (Nageotte).

according to some, formed by the proteins of the myelin enclosing the fat substances. When the latter are dissolved, the former can be rendered visible. In this sense, the Schmidt-Lantermann incisures and the spirals of Rezzonico-Golgi are also preexisting formations. The former, for instance, are, according to Nemiloff, merely the thicker trabeculae

of the neurokeratin net and, like the spirals of Rezzonico-Golgi, can be rendered visible by special staining methods.

The myelin contains minute droplets or granules described as Elzholz bodies (fig. 2) and μ granules of Reich. The former, often the size of an erythrocyte, may be found between the myelin and the membrane of Schwann and also within small vacuoles of the Schwann cell itself. According to Doinikow, the μ granules are also myelinic, identical with the bodies of Elzholz, and are mainly enclosed within the cells of Schwann. Here are also present so-called π (protagonoid) granules, which are comma-shaped formations staining metachromatically (reddish violet) with thionine, toluidine blue and similar stains. In some animals the foregoing granules may be found in larger, in some in smaller, amounts; in some they are absent, but in pathologic conditions their amount is usually increased.

Whatever the significance of the structures observed in the myelin sheath, the fact is that the latter is enveloped by a group of branching

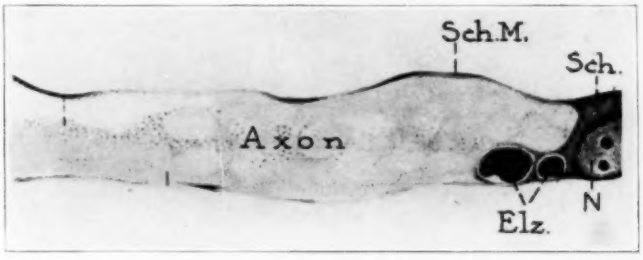

Fig. 2.—A peripheral nerve fiber from a dog. *Elz.* indicates Elzholz' bodies; *Sch.*, Schwann cell, increased in size; *Sch.M.*, Schwann membrane emanating from the former; *N.*, nucleus; the axon is granular; the myelin appears as a network (Doinikow).

cells of Schwann. Outside these lies another structure known as the membrane of Schwann. In contrast to the former, it is acellular, structureless and homogeneous, and it extends from one internode to another, but is not adherent to the adjacent tissues. It is considered by some (Nemiloff [7] and Reich [8]) to be an independent organ which has nothing to do with the subjacent syncytial membrane of Schwann cells. One must concede that it is not easy to establish the exact relationship between the Schwann cells and the Schwann membrane. Held and Nageotte look on it as a membrana limitans which separates the parenchyma of the nerve from its mesodermal constituents. The excellent drawing of Doinikow (fig. 2), as well as the figures from my speci-

8. Reich, F., in discussion on Boeke: Verhandl. d. Gesellsch. deutsch. Nervenaertze **20**:203, 1931; Deutsche Ztschr. f. Nervenh. **116**:35, 1930; Neurol. Centralbl. **29**:89, 1910.

mens (fig. 3), prove that the membrane is a part of the Schwann cell. It gives off lateral branches, which, at regular intervals, envelop the myelin (fig. 3). It plays a great rôle in pathologic conditions, in which it is greatly aided by an externally situated (fig. 4) mesodermal membrane. This consists of parallel connective tissue fibers, each fiber being enveloped by endothelial cells (Häutchenzellen of Key and Retzius [9]) and containing oblong nuclei, rich in chromatin. This layer, usually described as the membrane of Henle, subsidiary sheath of Ruffini or fibrillary membrane of Key and Retzius, is confined to the endoneurium and might as well be termed endoneural. Stöhr [10] considered the name

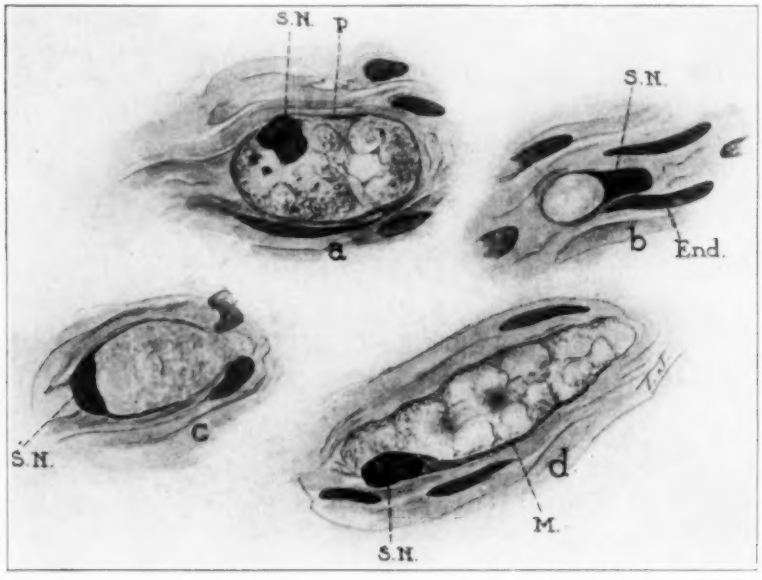

Fig. 3.—In *d* at *M.*, the Schwann membrane is emanating from the Schwann cell, which contains a large chromatin-rich nucleus (*S.N.*). With the opposite Schwann membrane, it encloses swollen myelin. The other three figures (*a*, *b* and *c*) show large Schwann nuclei (*S.N.*), the large processes (*P*) enveloping swollen and broken up myelin in the early stages of secondary degeneration. The oblong nuclei (*End.*) are hypertrophied endoneural cells.

Henle's membrane superfluous. It corresponds, he stated, to the fine perineural covering of the finest peripheral nerve bundles. By some it

9. Key and Retzius: Studien in der Anatomie des Nervensystems und des Bindegewebes, Stockholm, P. A. Norstedt & Söner, 1876, vol. 2.

10. Stöhr, Jr., P.: Die peripherische Nervenfaser, in Möllendorf, W.: Handbuch der mikroskopischen Anatomie der Menschen, Berlin, Julius Springer, 1928, vol. 2.

is also called neurilemma (Cajal [11] and Boeke [12]), a name also applied to the Schwann cells and the Schwann membrane. The confusion in the nomenclature, one must admit, is great, and it would be preferable to drop the name "neurilemma" altogether.

GENERAL PHENOMENA IN PATHOLOGIC CONDITIONS OF NERVE STRUCTURES

The uncertainty as to the anatomicophysiologic significance of various nerve structures must of necessity be apparent in pathologic conditions —in the degeneration and inflammation of nerves. The general phenomena occurring in these states may generally be classified as passive and active. The passive phenomena occur in the parenchymatous

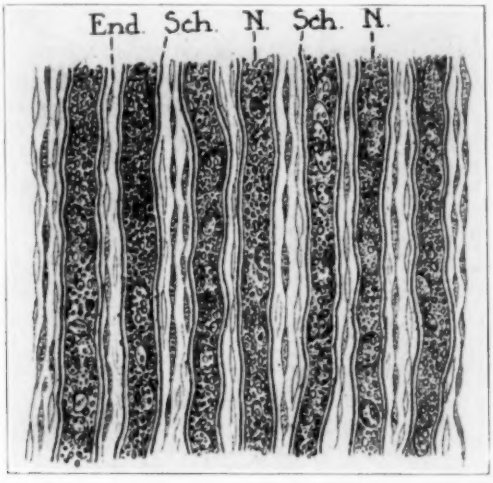

Fig. 4.—Longitudinal section of a nerve fiber, somewhat diagrammatic. *N.* indicates nerve parenchyma (axon and myelin) bordered by Schwann membrane (*Sch.*), and outside the latter is the endoneural, mesodermal (Henle's) membrane (*End.*). Between some nerve fibers are two endoneural membranes, one for each nerve; together with the blood vessels and various cell elements they form the endoneurium of a peripheral nerve. (After Hjelt.)

(axon and myelin) portions of a nerve fiber; the active phenomena are displayed in the surrounding membranes—the cells and the membrane of Schwann and the mesodermal sheaths, which transform the damaged or destroyed parenchyma into transportable and absorbable substances.

11. Ramón y Cajal, S.: Degeneration and Regeneration of the Nervous System, translated by Raoul M. May, London, Oxford University Press, 1928.

12. Boeke, J.: Studien zur Nervendegeneration, Verhandel. d. k. Akad. v. Wetensch. (Tweede Sectie), 1916 and 1917, no. 5; Ergebn. d. Physiol., 1921, vol. 19.

Passive Phenomena.—According to some observers, these changes show first in the myelin; according to others, they occur first in the axon. Probably the changes take place in both structures simultaneously, being occasionally more marked in one than in the other. In inflammatory and degenerative conditions they are practically alike, differing only in intensity and their course. In neuritis, for instance, the changes are, for a long time, confined to the myelin; the axon becomes involved much later, when a condition of secondary or wallerian degeneration [13] obtains. The early myelin changes seen in experimental conditions, twenty-four hours after section of a nerve, are mainly in the form of Elzholz bodies which, as mentioned, are, like the μ and π granules, of no great pathologic significance. In the later stages, the myelin at the incisures of Schmidt-Lantermann breaks up into fragments (ovoids, ellipsoids) and subsequently into drops, droplets and granules.

The early changes in the axon show: granular appearance (fig. 2), poor stainability and fragmentation into minute particles enclosed within digestive chambers of the myelinic ellipsoids. The breaking up of both the myelin and the axon results in the formation of chemical substances, so-called "Abbau" or catabolic products. The latter gather first in the cells of Schwann as myelinoid substances or lipoids. These soon appear as fat infiltrations in the adjacent endoneural membrane; still later they accumulate in the perineurium and epineurium, where they remain indefinitely until finally removed by the blood vessels.

Active Phenomena.—The attention of investigators was for some time centered on the myelin and axon; very little, if any, consideration has been paid to the condition of the surrounding membranes—Schwann cells, Schwann sheaths and the mesodermal membranes. Yet the latter play an important rôle in the processes occurring in pathologic nerves. They all, especially the cell membrane of Schwann, exhibit changes early (on the third day, according to Büngner). The cytoplasm increases in size (fig. 2); the processes become longer and numerous (fig. 3); the vacuoles in the cytoplasm also increase in size and number, and become filled with droplets of myelin. They may be quite large and give the cells the appearance of myelophages (figs. 5 and 6), as described by Jakob in degeneration of the central nerve fibers. The myelophages become gradually transformed into so-called gitter cells (fig. 7), in which the vacuoles are all small, alike and filled with lipoid granules. The nucleus,

13. Waller, A.: Experiments on the Section of the Glossopharyngeal and Hypoglossal Nerves of the Frog and Observations of the Alterations Produced Thereby in the Structure of Their Primitive Fibers, Phil. Tr., London, 1850, pt. 1, p. 423; Sur la reproduction des nerfs et sur la structure et les fonctions des ganglions spinaux, Arch. f. Anat. u. Physiol., 1852, p. 392.

always misplaced to the periphery, is rich in chromatin. By careful study and analysis of a large experimental material, Doinikow was able to follow the gradual process of transformation of Schwann cells into fat granule bodies (gitter cells) harboring lipoid substances, the products of destroyed nerve tissue. In this stage of nerve degeneration, the normal constituents of a nerve fiber are absent. There is no myelin or

Fig. 5.—Early stages of nerve degeneration. *M* indicates swollen myelin; at M^1, broken fragments (Marchi balls) are enclosed within vacuoles formed by the Schwann membrane; *Sch.* indicates Schwann nuclei and processes emanating from them; *Sch.M.*, the Schwann membrane; *End.m.*, the endoneural membrane extending alongside the nerve; *End.n.*, endoneural cells; *My.*, myelophages. Bielschowsky stain; × 800. (From a specimen of a collection lent me by Professor Spielmeyer.)

axon; nor are there cells or membranes of Schwann. They all become transformed into gitter cells, which enclose the nerve tissue transformed into lipoids (figs. 7 and 6). Instead of a nerve there is a hollow tube.

Its contents are mainly the foregoing fat granule bodies; its walls are the hypertrophied and hyperplastic endoneural membrane. The latter exhibit a marked reaction in very early stages, but somewhat later than the cells of Schwann. As figure 3 shows, the cells and the membrane of Schwann, emanating from the former, envelop the swollen fragments of the myelin and are bordered by hypertrophied chromatin-rich nuclei of the endoneural cells. The capillaries become engorged and prominent, and their endothelial nuclei large and tumefied.

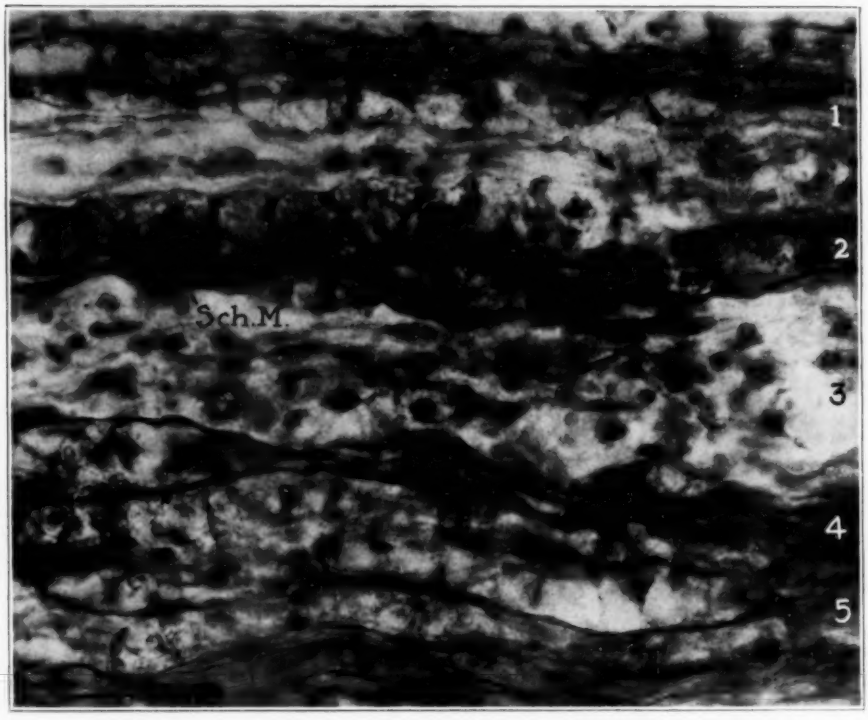

Fig. 6.—Five degenerated nerve fibers in various stages of degeneration are indicated by numbers. The process of degeneration is generally here farther advanced than in the previous photograph. The thick black lines are Schwann membranes (*Sch.M.*); in nerve *2*, and less distinctly in the other nerves, processes are given off dividing and enveloping granular-appearing fragments (formation of myelophages); at *3* is a more advanced stage; gitter cell formation can be discerned at *4* and *5*. Bielschowsky stain; × 540. (From a specimen of a collection lent me by Professor Spielmeyer.)

According to Doinikow,[6] the proliferative mesodermal phenomena reach their height during the second or third week. The Schwann and many mesodermal cells become vacuolated and are gradually transformed into gitter cells packed with lipoids, so that, in late stages, the

endoneurium, perineurium and epineurium exhibit cell elements similar to those present within the hollow tubes of the nerve fibers. They may predominate outside the latter, among the cells of the endoneural spaces. These appear very cellular; the numerous homogeneous, spindle-shaped endoneural cells become large, hypertrophied, often vacuolated and mixed with rather small branching fibroblasts and fat-granule bodies

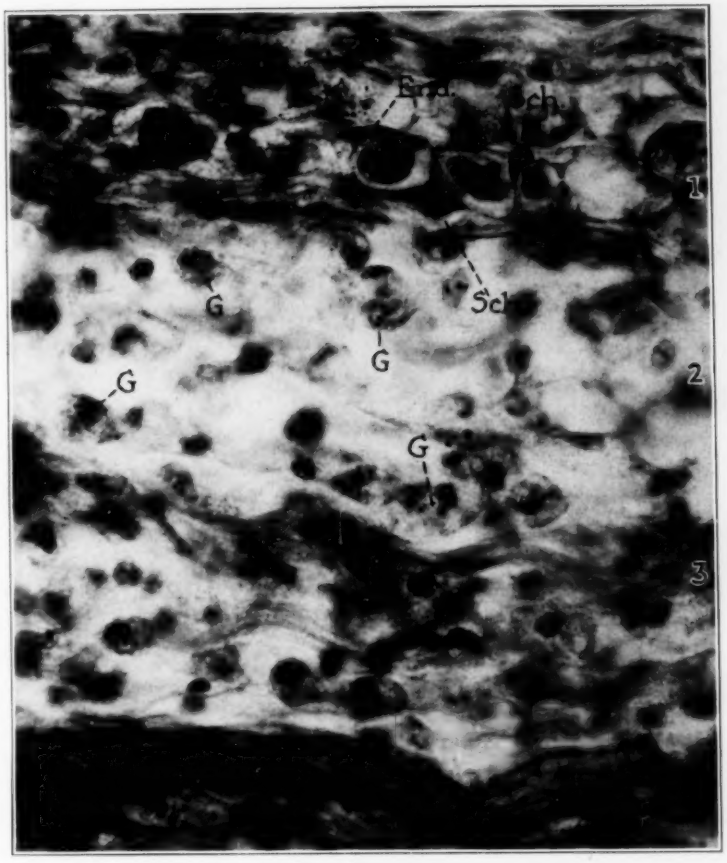

Fig. 7.—At *1* are seen Marchi balls or broken up myelin (black fragments) within vacuoles formed by processes of cells of Schwann (*Sch.*); at *2*, gitter cells (*G, G, G*) have replaced a nerve fiber; *End.* indicates endoneural cell; at *3*, the gitter cells are mixed with endoneural cell elements. Bielschowsky stain.

packed with lipoids. The foregoing elements are present within the endoneurium, perineurium and epineurium, the products of the degenerated nerves being, as shown by Doinikow, successively removed, together with the modified Schwann and endoneural cells enclosing them, from the place of destruction to the outer membranes—the perineurium

(fig. 9) and epineurium—for final elimination by the blood vessels. They may also be found in the dilated perivascular (fig. 9) spaces of the blood vessels of the nerve membranes. The result is that the peripheral stump is ultimately deprived not only of its myelin and axon but also of the Schwann cells, which, having been transformed into gitter cells, have ceased to exist (fig. 10).

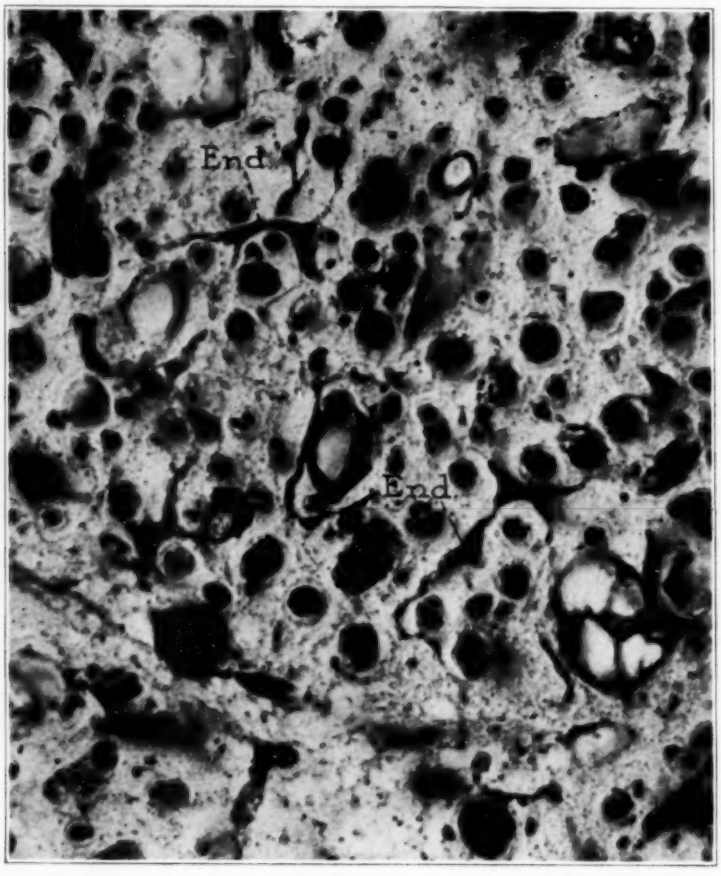

Fig. 8.—Among the degenerated nerve fibers are hypertrophied, branching endoneural cells (*End.*), much resembling microglia; × 1,000. (From a specimen of a collection lent me by Dr. Ranson.)

Spielmeyer [14] maintained that the Schwann cells remain in the syncytium after they have given up their fat. Edinger was of the same

14. Spielmeyer, W.: Ueber Regeneration peripherischer Nerven, Ztschr. f. d ges. Neurol. u. Psychiat. **36**:421, 1917; in Bethe: Handbuch der normalen und pathologische Physiologie, Berlin, Julius Springer, 1929, vol. 9, p. 285.

opinion, adding that after giving up the fat the phagocytic Schwann cells shrink and become reduced to spindles. Situated along the course of the nerve fibers, they are gradually transformed into long cordons or bands of Büngner. Nageotte held that the phagocytosis is done by macrophages coming from outside after penetrating the Schwann membrane. According to Bielschowsky,[15] again, only some Schwann cells are trans-

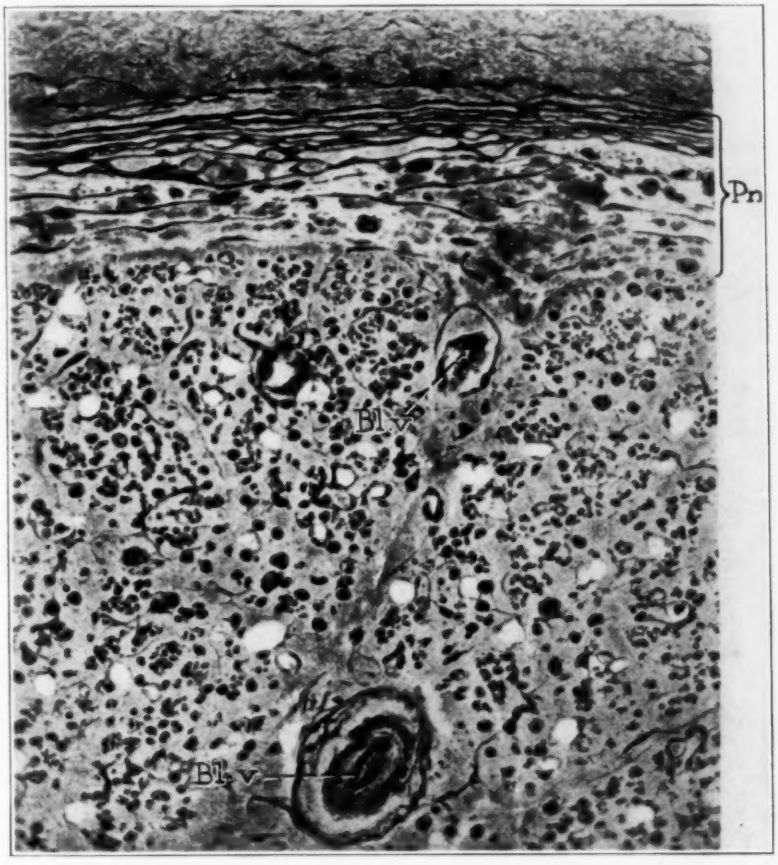

Fig. 9.—Transverse section of a dog's nerve (from specimens of a collection lent me by Dr. Ranson). The nerve fibers are degenerated and greatly reduced in number. The degenerated products can be seen in the interlamellar spaces of the perineurium (*Pn*) as darkly stained gitter cells; at *Bl.v.* is a blood vessel with a ringlike, dilated space. Pyridine silver stain; × 300.

formed into so-called "Abbau" cells, while others remain in situ, forming Büngner's cell cordons. In the specimens I studied, the only cells that

15. Bielschowsky, M., and Unger, E.: Die Ueberbrückung grosser Nervenlücken, J. f. Psychol. u. Neurol. **22**:267, 1917.

remained were proliferated endoneural cells (fig. 10). Some of the latter, which may gather in immense numbers (in Edinger's [7] experiments there were "clouds" of them), may, as said, be transformed into gitter cells, but the majority remain in situ, forming cell cordons or bands. Like some investigators before and many after him, Büngner [16] assumed that the latter are made up of cells of Schwann that have proliferated by mitosis. Their cytoplasm assumes, according to him, a fibrillary structure that gives rise to longitudinal stripes densely covered by nuclei and from which new axons develop. The newly formed axons arise discontinuously, each Schwann cell forming independently, as it

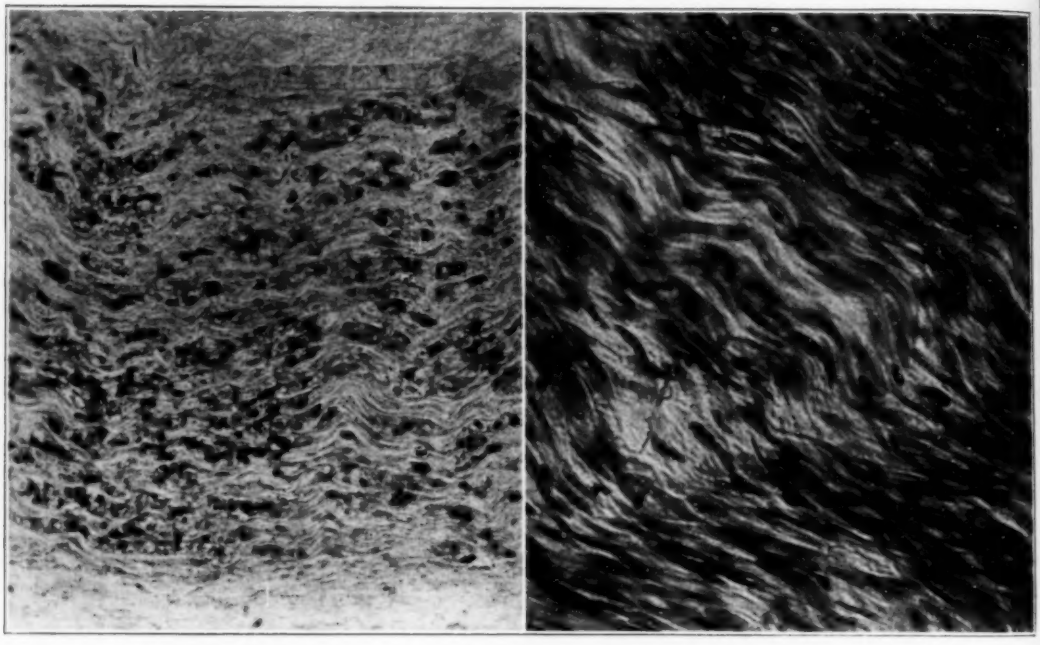

Fig. 10.—The dark masses in the picture on the left (scarlet red stain) are gitter cells filled with lipoids, the sole remnants of degenerated nerve fibers; the pale wavy lines are bands of mesodermal, endoneural fibers which are generally pictured as Schwann cell cordons of Büngner. To the right the same are stained with hematoxylin-eosin; reduced from a magnification of × 700. (From a specimen of a collection lent me by Professor Spielmeyer.)

were, a new nerve fiber. Chains of young nerve fibers thus arise, which may become ripe only after they have reached their center, the ganglion cells; otherwise, they degenerate. The ability of Schwann cells to create nerve fibers is, according to Büngner, due to their supposed neuro-

16. Büngner, Otto: Ueber die Degenerations—und Regenerations—Vorgänge an Nerven nach Verletzungen, Beitr. z. path. Anat. u. z. allg. Path. **10**:321, 1891.

blastic or neurogenic nature. Thus was created the peripheral, discontinuous, catenary theory of nerve regeneration,[17] which gave rise to many heated controversies between neuronists and antineuronists. It would be superfluous to take up the arguments advanced by either school. The main features are: the admission by the antineuronists that the discontinuously formed nerve fibrils mature only when they become connected with the center; their failure to consider the tremendous producing power of the central stump with its mass of new fibrils, such a phenomenon being absent in the peripheral stump, and the fact that Schwann cells all disappear from the degenerated peripheral nerve stump and thus cannot give rise to the formation of new fibers.

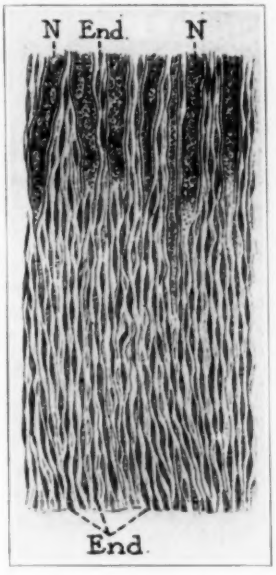

Fig. 11.—The normal nerves (*N, N*) in the upper part of the picture with the endoneural membranes (*End.*) are replaced in the lower part by bands that are continuous with the endoneural cells above. (After Hjelt.)

It has been considered (Spielmeyer) that the Schwann cells packed with lipoids do not leave the nerve fiber after they give up their lipoids, but remain in situ and evidently resume their original shape and function. Such a condition is hardly conceivable, for a Schwann cell once changed structurally is no longer a Schwann cell but a phagocyte that perishes together with its contents. As noted, nothing is left of the nerve, except rows or cordons of spindle-shaped endoneural cells (fig. 10). The Schwann cells seen in the peripheral sector over the nerve

17. Bethe, A.: Allgemeine Anatomie und Physiologie des Nervensystems, Leipzig, Georg Thieme, 1903.

fiber are outgrowths from the central stump, whence they came down, accompanying the sprouting axon (fig. 12). As figure 12 *B* shows, the cells are situated between the nerve fiber and the rows of endoneural cells, and morphologically, they may so much resemble the latter that a differential diagnosis, as Doinikow pointed out, is possible only with specific stains. Closely adjacent to the nerve fibers (fig. 12 *B*) such cells in the peripheral stump are decidedly less numerous than the masses of the endoneural cells, being, as said, most likely outgrowths from the Schwann cells of the central stump.

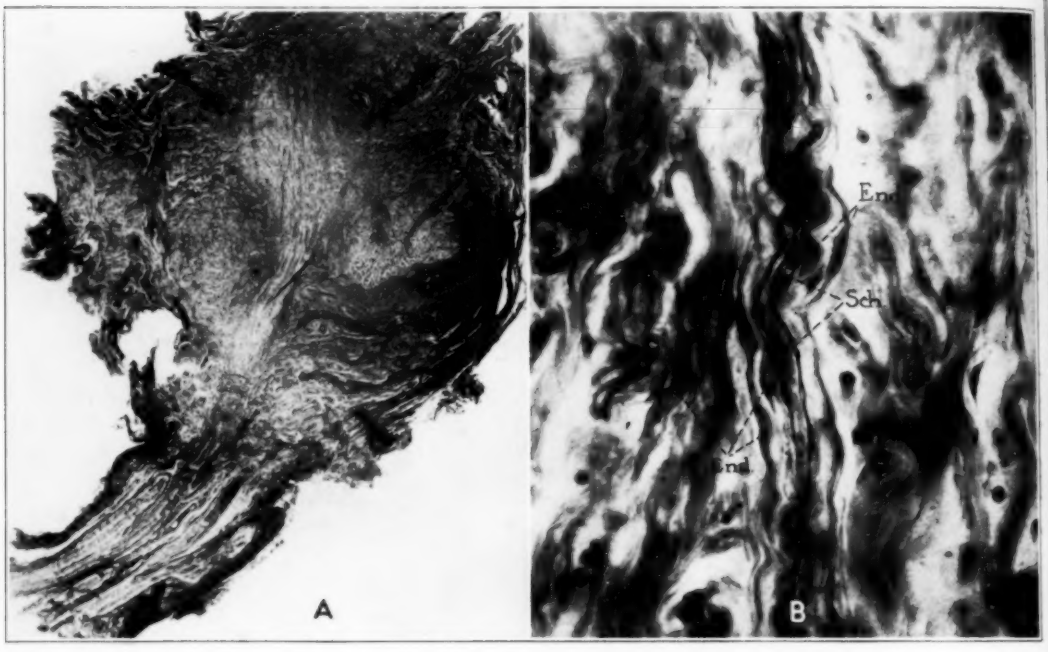

Fig. 12.—*A* shows the central stump of a connective tissue scar entering a "neuroma"; *B*, regenerating nerve fibers (dark wavy lines) closely covered by Schwann cells (*Sch.*) and rows of endoneural fibers (*End.*) forming tubes and running parallel. (From a specimen of a collection lent me by Professor Spielmeyer.) Bielschowsky stain; reduced from a magnification of × 700.

Figure 11, taken from Hjelt,[18] may be considered a good illustration of what actually takes place. The junction of the endoneural cells of the upper segment, containing preserved nerve fibers, with similar cells of the periphery leads to the formation of continuous bands as presented in this picture. At the periphery, they monopolize the field and form parallel tubes, being a manifestation of a mesodermal nerve reaction.

18. Hjelt, O.: Ueber die Regeneration der Nerven, Virchows Arch. f. path. Anat. **19**:352, 1860.

This also shows in the perineurium and epineurium. The former is made up of distinct circular lamellae (fig. 9), each lamella being covered by flat endothelial cells (Häutchenzellen or membranous cells of Key and Retzius). The interlamellar spaces are in communication with the endoneural spaces. In nerve lesions, they are not only very vascular, but also, as figure 7 shows, very cellular, containing among other cells numerous fat-granule bodies (gitter cells) transported there from the

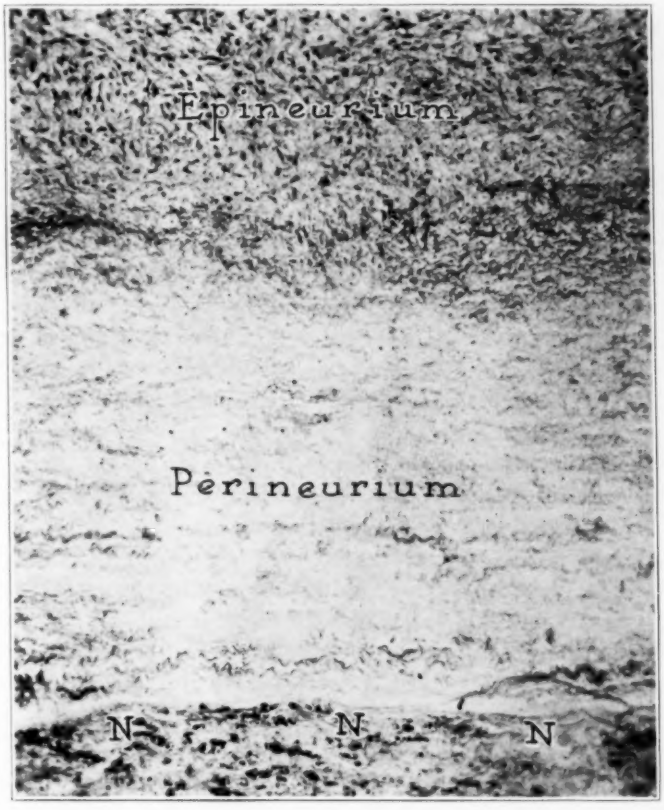

Fig. 13.—*N*, *N* and *N* indicate degenerated nerves; the epineurium shows marked cellular hyperplasia. Bielschowsky stain; × 65. (From a specimen of a collection lent me by Dr. Ranson.)

endoneurium. The type of cells seen in the latter are, as mentioned, also present in the perineurium and epineurium which, like the endoneural membrane, exhibit phenomena of cell hypertrophy and cell hyperplasia (fig. 13). The proliferated spindle cells of the mesodermal membranes join those of the terminal portion of the central nerve stump, resulting in the formation of pathways that guide the outgrowing regenerating central nerve fibers (fig. 11).

According to Cajal and his school, the outgrowing fibers pass down in spaces between rows of cells, while Ranson,[19] Boeke,[20] Bielschowsky,[15] Spielmeyer [14] and others speak of intraplasmatic growth, the nerve fibers growing within the cytoplasm of the cell cordons. The school of Cajal also maintains that the outgrowth of young fibers is free. Later they become invested by Schwann cells, while Boeke, though an advocate of the centrogenic theory, does not accept free growth of nerve fibers. These are always invested with a fine membrane of Schwann cells extending from the central stump.

A number of clinical and pathophysiologic facts decidedly favor the central theory of nerve regeneration. Of the pathophysiologic facts, the most convincing is the growth of immense numbers of new fibrils from the central stump and their invasion of the scar that connects the central and peripheral stumps of a divided nerve. Such an outgrowth is not seen in the peripheral stump. In his splendid contributions on nerve degeneration and regeneration, Boeke showed that fibrillary twitchings of an atrophied tongue following section of the twelfth nerve disappear, together with the atrophy, after the outgrowing central stump reaches the muscular fibers. On the other hand, in poliomyelitis, bulbar paralysis and similar conditions, essentially central nerve lesions, degeneration of the entire peripheral neuron is the inevitable result, as if the fibers had been artificially separated from their center. Were an independent regeneration of a peripheral stump possible, poliomyelitis and kindred diseases would be curable. The same is true of amyotrophic lateral sclerosis, multiple sclerosis and other conditions due to central nerve lesions. The latter do not regenerate, even when the obstruction, dividing nerve fibers from the center, is removed. The cause of the failure of the central nerve fibers to regenerate was looked for in the absence of Schwann cells and a Schwann membrane. The former, however, may be represented in a central nerve fiber by numerous glia nuclei, known as oligodendroglia, the structureless Schwann membrane and the endoneural sheath being here absent. The mesodermal cells scattered among the central nerve fibers do not form around them a solid membrane after they have performed the phagocytic function of digesting and removing the damaged nerve fibers, as is the case at the periphery. In addition, the proliferation of the cytoplasmic glia, capillaries and blood vessels inevitably leads in the brain, at least in disseminated cerebrospinal lesions, to the formation of numerous microscopic scars, which form obstacles to the possible growth of young nerve fibers. New fibers probably do

19. Ranson, S. W.: Degeneration and Regeneration of Nerve Fibers, J. Comp. Neurol. **22**:487, 1912.

20. Boeke, J.: Die Regenerationserscheinungen bei der Verheilung von motorischen und rezeptorischen Nervenfasern, Arch. f. d. ges. Physiol. **128**:84, 1914; footnote 12.

form, but either their number is not sufficient or the young fibers are neither strong nor powerful enough anatomically and physiologically to replace the old, damaged ones. Even in peripheral nerves that have been most carefully sutured recovery is hardly complete (Cajal), and in the presence of scars it is either altogether deficient or may fail completely. On the other hand, a sutured divided peripheral nerve may recover within a rather short time; in several days, for instance. This is difficult to explain, for, if the fibers growing from the central stump invaded the periphery only after the latter had undergone complete degeneration and become replaced by cordons of cells, a recovery of function could not be expected in several days or weeks as it has been claimed for some cases. Perroncito [21] thought that rapid recoveries in such cases depend on the presence of collaterals. He himself, however, never saw instances of rapid recovery of nerve function. The undisputed fact is that when the divided stumps of a nerve are sutured, the comparatively early restoration of function is practically assured. It is hard to give the reasons. Probably, when the mesodermal membranes are sutured, the outgrowing fibers are given better facilities for concentrating within a limited space, and thus do not go astray. They are not only directed but also protected by the enveloping connective tissue structures. The protection is in the form of aiding both the metabolism and the catabolism of the numerous young fibers that stream down from the center. In other words, there must be some relationship—anatomic and functional—between the active young growing fibers and the surrounding mesodermal formations. Such a relationship may be better understood if one considers that existing between the adult nerve and its envelopes.

All the bundles of a peripheral nerve are enveloped by a common connective tissue membrane (epineurium). Being rich in fat and connective fibrous tissue, the epineurium represents an extension of the cerebrospinal dura. Prolongations of the epineurium into the depth of the nerve give off envelopes to each fasciculus of the latter, termed perineurium. Like the former, this is very vascular. According to Key and Retzius, it is a prolongation of the cerebrospinal arachnoid membrane. As endoneurium it invades the smallest bundles, or the fasciculi, sending membranes to each individual nerve fiber, the previously discussed endoneural sheaths. One thus finds in a peripheral nerve the same membranes as are present over the spinal cord or brain, excepting the pia. This does not extend over the periphery, but rather extends into the interior of the spinal cord, forming funnel-like prolongations carrying the blood vessels. On the other hand, the dura and arachnoid not only invest the

21. Perroncito, A.: Die Regeneration der Nerven, Beitr. z. path. Anat. u. z. allg. Path. **42**:354, 1907; Ueber die Zellen beim Degenerationsvorgang der Nerven, Folia neuro-biol. **3**:185, 1909.

brain and spinal cord but carry along, over the outgoing cerebral and spinal nerves, the enclosed subdural and subarachnoid spaces. By injecting the latter two spaces, Key and Retzius [22] were able to prove the existence of a communication between them and the perineural nerve spaces, and they concluded that the lamellae of the perineural sheath are continuous with those of the cerebrospinal arachnoid tunic. Injection of a peripheral nerve brings the injected fluid into its endoneural, perineural (interlamellar) and epineural spaces; from the latter the fluid reaches the spaces around the spinal ganglia, and from there the subdural and subarachnoid spaces of the spinal cord. Vice versa, injections into the spinal subdural and subarachnoid spaces following the foregoing pathways reach the perineural spaces of the nerves. An interruption of the latter by epidural lesions, such as epidural tumors, peripachymeningitis or other epidural inflammatory conditions as they occur in syphilis, for instance, must of necessity affect the flow of the spinal fluid and the spinal cord. This phase, discussed in a number of contributions,[23] confirmed the work of Key and Retzius that the neural membranes and their enclosed spaces are continuations of similar spaces of the brain and spinal cord—that the cerebrospinal fluid is drained by the perineural spaces of the cerebrospinal nerves.

A most striking confirmation of such a view has been furnished by the work of Funaoka [24] and his collaborators. On injecting dekahydrogen naphthalene, machine oil or similar substances into the peripheral nerves with a common Luer syringe and under a "very slight" pressure, Funaoka found the injected oil and various coloring substances suspended in it in the subarachnoid spaces of the cord and brain, and even in the cerebral ventricles. With Yamada, said Funaoka, by injecting about 25 cc. of dekahydrogen naphthalene stained with ultramarine into the peroneal nerve, he could stain almost the entire central nervous system of a middle-sized rabbit and "naturally quite well" the central nervous organs. Any nerve can be injected under mild pressure, the time of injection being sometimes not more than one-half hour. On microscopic examination, the injected fluid was found in the epineural and perineural spaces of the nerves and also in the brain, mainly in its subarachnoid and subdural spaces. Downward injections into one vagus

22. Key and Retzius: Studien in der Anatomie des Nervensystems, Arch. f. mikr. Anat. **9**:308, 1873; footnote 9.

23. Hassin, G. B.: Circumscribed Suppurative (Nontuberculous) Peripachymeningitis, Arch. Neurol. & Psychiat. **20**:110 (July) 1928; Disseminated Sarcomatosis (Melanoblastoma?) of the Central Nervous System and the Meninges, ibid. **21**:1087 (May) 1929; Tabes Dorsalis, ibid. **21**:311 (Feb.) 1929.

24. Funaoka, S.: Untersuchungen über das periphere Nervensystem: Die Injektion des Nervensystems, Kyoto, Japan, Anatomical Institute of Kyoto Imperial University, 1930, series A, no. 1.

caused the colored mixture to appear on the opposite side. On injecting lamp black into the peripheral nerves, the Japanese investigators demonstrated its occasional presence within the ventricles, often at the base of the medulla and around the basilar nerves, causing obstruction of the subarachnoid space and internal hydrocephalus as a result.

The foregoing studies, together with the famous experimental work of Key and Retzius and the pathologic observations already referred to,[23] show that the subdural and subarachnoid cerebrospinal spaces are continuous over the posterior roots, extending to the very periphery of the craniospinal nerves. No culdesacs or reflections exist over the spinal roots or elsewhere, as has been maintained in textbooks and monographs.[25]

The neural membranes and the spaces within them not only protect the nerves against injury and provide them with nutrition and warmth, but also assist in the discharge of the cerebrospinal fluid. An additional function is to assist in the repair of peripheral nerve injuries. Through their function, the metabolism in the peripheral nerves is thus much better sustained and rendered much more favorable than in the central nerve fibers. In the latter, the conditions of nutrition are not as good as in the peripheral nerve fibers, in spite of the presence of numerous blood vessels, protoplasmic and fibrous glia, and microglia. They lack the organized syncytial structures provided by the Schwann membrane and the mesodermal (endoneural and perineural) sheaths, which are essential to the circulation of the tissue fluids and the removal of catabolic products. The latter must of necessity form in large masses because of the activity of an enormous amount of young fibers. These products are easily eliminated by the well formed membranes and their spaces which, in the brain, are lacking. Their absence thus renders the conditions for nerve regeneration in the central nervous system extremely unfavorable. Attempts at regeneration are probably present but, as Howell and Huber [26] have put it, they are rather abortive.

CONCLUSIONS

1. The structure of a peripheral nerve fiber is more complex than that of a central fiber.

2. The Schwann cells and the Schwann membrane form one structure.

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25. Sicard, J. A., and Cestan, R.: Étude de la traversée méningoradiculaire au niveau du trou de conjugaison: Le nerf de conjugaison, Bull. et mém. Soc. méd. d. hôp. de Paris **21**:715, 1904. Elman, R.: Spinal Arachnoid Granulations with Especial Reference to the Cerebrospinal Fluid, Bull. Johns Hopkins Hosp. **34**:99 (March) 1925.

26. Howell and Huber: A Physiological, Histological and Clinical Study of the Degeneration and Regeneration in Peripheral Nerve Fibers After Severance of Their Connections with the Nerve Centers, J. Physiol. **13**:335, 1892.

3. The Schwann membrane separates the parenchyma from the surrounding mesodermal tissues.

4. The Schwann cells undergo irreparable changes in wallerian degeneration and are, like the damaged parenchyma, removed from the place of the lesion.

5. As such cells cease to exist, new nerve fibers cannot be produced from them, as has been maintained by the antineuronists.

6. The Schwann cells seen in a peripheral sector evidently come from the central stump and accompany the outgrowing new fibers.

7. The endoneural cells growing in both central and peripheral stumps merge to form cell cordons, which constitute the proper conducting pathways for the outgrowing nerve fibers.

8. Such cordons not only assure proper pathways for the growing nerve fibers, but assist in their metabolism by removing the products of the latter.

9. The absence of such syncytial structures in the brain is probably the cause of the failure of central fibers to regenerate.

THE SYNDROME OF POLYNEURITIS WITH FACIAL DIPLEGIA *

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Since the World War, largely due to a comprehensive paper by Bradford, Bashford and Wilson, there has been renewed interest in what has generally been termed infectious polyneuritis. The credit for bringing this condition to attention has frequently been given to Osler,[1] who in the first and subsequent editions of his textbook, under the general subject of neuritis, described briefly what he termed "acute febrile polyneuritis." There is little doubt that his account of the disease corresponds in a general way with what has more recently been described under a great variety of names. He considered one of the essential features to be a considerable rise in temperature at the onset and evidences of an acute infection followed by general neuritic symptoms with possible extension to the muscles of the face. It is evident, however, that this was by no means the first description of the disorder.

Laurans,[2] in a doctorate thesis published in 1908, covered completely the knowledge of the subject up to that date. He cited the fact that Pierson, in 1869, discussed the subject of facial diplegia and difficulty with movement of the legs. During the decade from 1870 to 1880, the relation of peripheral neuritis and double facial paralysis came to be recognized, and beginning in 1888 the possible infectious-toxic origin of these conditions was suggested. Laurans was able to collect eighteen cases in which double facial paralysis was associated with neuritic signs and symptoms, and he gave a general description of the condition which is in many respects satisfactory today. He drew attention, as did Osler, to the possibility of confusing the condition with so-called Landry's paralysis, and concluded that the disorder was unusual but not extremely rare.

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* Submitted for publication, June 29, 1931.

* Read at the Fifty-Seventh Annual Meeting of the American Neurological Association, May 28, 1931.

1. Osler, William: The Principles and Practice of Medicine, ed. 1, New York, D. Appleton & Company, 1892, p. 777.

2. Laurans, A.: Thèse de Paris, 1908, p. 156.

In 1894, Targowla [3] gave a detailed description of a case of polyneuritis with facial diplegia entirely analogous to those later described. Although making no reference to facial paralysis, Walton,[4] in 1895, published a paper that is interesting in connection with later developments in which he attempted to demonstrate that what had been called Landry's paralysis was in reality presumably a type of neuritis, making the statement that he believed Landry's paralysis would cease to be regarded as a distinct entity. The frequent mention by later writers of the confusion existing between infectious polyneuritis and the symptom complex of Landry's paralysis is suggestive.

A typical case of a combination of polyneuritis and paralysis of the facial nerves was published by Sinnegar [5] in 1899. The whole subject was reviewed by Patrick [6] in 1916 under the caption "Facial Diplegia in Multiple Neuritis"; he added twenty-nine cases gathered from the literature in addition to two of his own to the eighteen that Laurans had previously collected. Thomson,[7] in 1910, added a personally observed case.

In 1917, Gordon Holmes,[8] using Osler's terminology "acute febrile polyneuritis," described the cases of twelve patients observed in war practice and gave the symptomatology in detail. Two of the cases were studied post mortem.

As already indicated, the most significant paper on the subject is that of Bradford, Bashford and Wilson,[9] published in 1918 on the basis of thirty cases observed among the soldiers in France. Twenty of these are carefully reported. Apart from the excellent clinical description of the symptomatology, this paper is important, as a more detailed account than was hitherto available is given of the pathologic changes both in man and in experimental monkeys. Even more important than this is the claim that the virus was cultivated, its character in general established and organisms recovered post mortem from inoculated animals.

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3. Targowla, J.: Polynévrite recidivante, envahissement des nerfs craniens et diplégie faciale, Rev. neurol. **2**:465, 1894.

4. Walton, G. L.: Multiple Neuritis the Essential Element in Landry's Paralysis, Boston M. & S. J. **133**:637, 1895.

5. Sinnegar, H.: A Case of Paralysis of Both Facial Nerves with Some Affection of the Limbs, from Peripheral Neuritis: Recovery, Brit. M. J. **2**:138, 1899.

6. Patrick, H. T.: Facial Diplegia in Multiple Neuritis, J. Nerv. & Ment. Dis. **44**:322, 1916.

7. Thomson, F. G.: Acute Toxic Polyneuritis, Brit. M. J. **2**:1443, 1910.

8. Holmes, Gordon: Acute Febrile Polyneuritis, Brit. M. J. **2**:37, 1917.

9. Bradford, J. R.; Bashford, E. F., and Wilson, J. A.: Acute Infective Polyneuritis, Quart. J. Med. **12**:88, 1918.

In 1919, Kennedy [10] suggested the term infective neuronitis rather than polyneuritis, recognizing that the lesions were far more extensive than the simple term neuritis would imply. In the same year, Casamajor described the pathologic lesions under the simple title "Acute Ascending Paralysis Among Troops."

In 1920, Bassoe [11] suggested the possible relationship of encephalitis to this type of infectious neuritis. He noted particularly pial inflammation over the cerebral cortex in the case studied by him. He stated that facial paralysis occurred, although it was not a marked feature.

Govaerts,[12] in 1924, published a typical example of "polyradiculitis" and bilateral facial paralysis, with a careful study of the spinal fluid.

Barker, Cross and Irwin,[13] in the same year, described this general group of conditions with special reference to encephalitis, using the term "meningo-encephalo-myelo-neuritis."

In 1927, Viets [14] reported a fatal case with pathologic changes in the nucleus of the seventh nerve and in the ventral horns of the cord.

In the last decade, other papers have appeared on the general subject by Skoog,[15] Sharkne and Moog,[16] Bériel and Devic,[17] Margulis,[18] Grainger Stewart,[19] Wilfred Harris,[20] François, Zuccoli and Montus,[21] Hendrick,[22] Strauss and Rabiner,[23] and Sands,[24] all of which appear to

10. Kennedy, F.: Infective Neuronitis, Arch. Neurol. & Psychiat. **2**:621 (Dec.) 1919.

11. Bassoe, P.: The Delirious and the Meningo-Radicular Types of Epidemic Encephalitis, J. A. M. A. **74**:1009 (April 10) 1920.

12. Govaerts, P.: Le syndrome de polyradiculite avec hyperalbuminose massive et xanthrochromie du liquide céphalo-rachidien, Scalpel, Sept. 6, 1924, no. 36.

13. Barker, L. F.; Cross, E. S., and Irwin, S. V.: Meningo-Encephalo-Myelo-Neuritis, Am. J. M. Sc. **159**:157, 1920.

14. Viets, H. R.: Acute Polyneuritis with Facial Diplegia, Arch. Neurol. & Psychiat. **17**:794 (June) 1927.

15. Skoog, A. L.: Multiple Neuritis, M. Clin. North America **7**:1323, 1924.

16. Sharkne and Moog: Ueber Beziehungen zwischen Neuritis und Encephalitis epidemica, Ztschr. f. d. ges. Neurol. u. Psychiat. **90**:89, 1924.

17. Bériel, L., and Devic, A.: Les formes périphériques de l'encéphalite épidémique, Presse méd. **33**:1441, 1925.

18. Margulis, S. M.: Myelo-Radiculo-Polyneuritiden bei epidemischer Encephalitis, Deutsche Ztschr. f. Nervenh. **89**:262, 1926.

19. Stewart, Grainger: Causation and Symptomatology of Multiple Neuritis, Brit. M. J. **2**:461, 1925; discussion by Harris, Wilson and others.

20. Harris, W., in discussion on Stewart (footnote 19).

21. François, M.; Zuccoli, G., and Montus, G.: Sur un cas polyradiculonévrite curable avec dissociation albumino-cytologique: Syndrome de Guillain et de Barré, Rev. neurol. **1**:95, 1929.

22. Hendrick, M. H.: Polyradiculonévrite avec dissociation albuminocytologique et paralysie faciale double, Rev. neurol. **36**:607, 1920.

23. Strauss, I., and Rabiner, A. M.: Myeloradiculitis, Arch. Neurol. & Psychiat. **23**:240 (Feb.) 1930.

24. Sands, I. J.: Acute Benign Infectious Myelitis, J. A. M. A. **96**:23 (Jan. 3) 1931.

belong in the general category of infective processes, though in some instances the facial nerves were not involved.

While recognizing the extensive and diversified infections of the nervous system, presumably induced by ultramicroscopic organisms, the whole subject is still in a formative stage and up to this time has hardly advanced beyond detailed clinical description and possible relationships. The radical conclusions regarding etiology reached by Bradford, Bashford and Wilson have not been, so far as is known, verified by other investigators.

TERMINOLOGY

To establish the condition outlined by Osler and others as a clinical entity is hardly to be seriously considered in the present chaotic state of knowledge. This is evidenced particularly by the nomenclature used in the attempt to describe this so-called disease.

Acute febrile polyneuritis is obviously unsatisfactory and not sufficiently inclusive, since it has become evident that the process involves the central nervous system far beyond the peripheral nerves. Polyneuritis with facial diplegia is inadequate for the same reason, although it stresses the frequently observed involvement of the facial nerves. Kennedy's terminology—infective neuronitis—is a commendable attempt to describe the condition more adequately from an anatomic standpoint, but is still insufficient.

Casamajor, despairing of an accurate designation, used the term acute ascending paralysis, which is perhaps somewhat misleading as it suggests Landry's paralysis, and also it is an inadequate phrase to explain the entire symptom complex.

Barker, Cross and Irwin have used the somewhat cumbersome term meningo-encephalomyeloneuritis, which has the merit of being a definite attempt to describe the condition so far as its location is concerned.

Bassoe spoke of meningoradicular types of disturbance. Margulis used the term myeloradiculopolyneuritis, and Strauss and Rabiner, myeloradiculitis.

The French writers Guillain, Francois and Hendrick prefer the term radiculoneuritis or polyradiculoneuritis, including the sign, described first by Guillain and his associates, of albuminocytologic dissociation (polyradiculo-névrite avec dissociation albumino-cytologique).

In the absence of a definite etiologic factor, which cannot be regarded as yet established, no entirely satisfactory terminology can be expected. Each of the terms suggested has distinct merit, but no one can be considered to cover the ground completely, as it is impossible to say what the actual condition, certainly from an etiologic standpoint, is which underlies the highly varying symptomatology of this large

group of little understood infections. It is the purpose of this paper to lay stress simply on the particular symptom complex of double facial paralysis and a condition that at least has neuritis as one of its essential features. It cannot be maintained, as some have thought, that this represents a definite disease entity, but it has been observed over so long a period of years and is so striking in its manifestations that at least one may regard it from the clinical standpoint as a reasonably constant association. Doubtless, in the future it will be found, as has happened in many other conditions, both in the nervous system and elsewhere, that a single underlying cause may lead to diverse manifestations under varying conditions of the body and its power of resistance.

In the following series of cases, therefore, only those are included which in addition to general neuritic signs had also a definite double facial paralysis.[25] That these cases have at times been misinterpreted and wrongly classified, often as so-called Landry's paralysis, is, for example, indicated by the following case, first observed by one of us (Dr. Taylor) in 1895, and published in April, 1900, under the caption "Landry's Paralysis: Remarks on Classification." [26]

A man, aged 52, was admitted to the Long Island Hospital, Boston Harbor, on Oct. 7, 1895. A month before, he had had what he supposed was malaria from which he recovered. Several days before entrance to the hospital, being as he supposed as well as usual, he stumbled and fell without loss of consciousness. That night he had pain in the back and dorsal leg muscles, together with a general sense of weakness and occasional sharp pain. There was no disturbance of the sphincters. A few days later he fell again and experienced the same feeling of weakness that he had had before. He was, however, able to walk with the aid of a cane. The weakness increased. On October 9, he began to have some difficulty in articulation and a gradually increasing inability to close the eyes. The following night, there was some regurgitation of food and considerable frontal headache. He was then unable to stand unsupported and complained of a sensation of numbness in the region of the epigastrium and said that "his skin felt dead" below the level of the umbilicus. On the following day he was excessively weak; the knee jerks were lost; there was no plantar reflex; the cremasteric reflex was absent on the right and present on the left; the abdominal reflexes and the leg and arm reflexes were normal. There was considerable fibrillary tremor of the abductors of both sides. There was no pain on deep pressure over the nerve trunks. The patient had a subjective sensation of cold, especially about the ankles. There was possibly a slight diminution of sensation to pinprick in the legs. The pupils reacted normally to light. There was double facial paresis, which was more marked on the right. The tongue could not be protruded beyond the lips; swallowing was difficult. Apart from these conditions, the cranial nerves were uninvolved. He had no fever, and physical examination otherwise gave negative results except for a pulse rate of 120. On October 12, the general weakness had further increased, and there was definite although slight sensory disturbance in the legs involving the temperature sense. There was also slight ataxia of the arms. An electrical examination gave

25. Case 13 and possibly case 12 are exceptions.

26. Taylor, E. W.: J. Nerv. & Ment. Dis. **27**:177, 1900.

negative results. On October 17, the pulse remained rapid, reaching 132. The facial paralysis was now practically complete. He had urinary and fecal incontinence. Mentally, the patient was clear and hopeful. He died on the same day, ten days after entrance and fifteen days after the onset of symptoms.

Necropsy.—An examination was made thirty-six hours after death. The brain, cord, viscera and the left pneumogastric, a portion of one sciatic and the left popliteal nerves were examined. The spleen was considerably enlarged (360 Gm.). There was no general arteriosclerosis, and except for a small focus of tuberculosis at the right apex the viscera were normal. Microscopic examination of the central nervous system showed nothing of significance except the presence of numerous hyaline bodies (amyloid) in various localities, a focus of tuberculous meningitis in the thoracic cord and pigmentary degeneration of numerous ventral horn cells. No definite degeneration was found in the peripheral nerves nor other evidence of meningeal change than that of the focus of tuberculous meningitis.

This case in onset, course and physical signs, except for retained deep reflexes, corresponds perfectly to those which later were described as infectious polyneuritis with facial diplegia. It was not recognized at the time since no such cases had hitherto been described. Laurans' thesis did not appear until 1908; in it the first systematic description of the disease was given. It is of some interest, in view of later publications, that this case was used as a text against the conception of Landry's paralysis as a distinct entity, although for want of a better term it was published under this caption.

Again, in 1903, a series of cases was reported by one of us (Dr. Taylor) under the title "Poliencephalomyelitis and Allied Conditions," [27] some of which are identical with the special type of disturbance under discussion and others closely related. The second case of this series was in brief as follows:

A man, aged 32, after a prodromal illness of undefined character developed a tingling sensation in the extremities and shortly afterward suddenly fell on account of increasing weakness. A practically complete paralysis of the legs quickly developed, with pronounced but less marked involvement of the arms. The sphincters were not impaired. Physical examination showed, in addition to the markedly paretic condition of the extremities, absent knee jerks without pronounced objective sensory loss and double facial paralysis together with paresis of the left sixth nerve.

This case undoubtedly belongs in the category under discussion. Another case reported in this paper was similar in the rapid onset of weakness of the legs and arms. Later, a definite paresis of the left seventh nerve developed, with a quantitative diminution of electrical excitability. This case suggested at the time the symptom complex of so-called Landry's paralysis. In both a fairly rapid and complete recovery took place. Other cases involving both facial nerves, without involvement of the spinal nerves, were likewise described as presumably constituting different types of the same infection, together

27. Taylor, E. W.: Boston M. & S. J. **148**:634, 1903.

with one in which a poliencephalitis superior and inferior was associated with a definite poliomyelitis involving the arms, as indicated by the fact that permanent atrophy remained after recovery in other respects.

At the time these cases were reported, about thirty years ago, it was presumed that they should be included in a general group of infections without sharp differentiation into separate entities, an assumption that has been rather accentuated since, in spite of more accurate and much extended clinical observation.

The following cases are therefore reported merely as an outstanding grouping of symptoms deserving separate consideration.

REPORT OF CASES

CASE 1.—An unmarried woman, aged 29, except for a localized neuritis in the left arm fifteen years before, had been well until the present illness. On Nov. 12, 1921, she gave the following history: Some weeks before, she had had a temperature of 102 F., and a tentative diagnosis of influenza was made. She had pain in the back and about the waist which subsided at the end of four days, with fever continuing for approximately ten days. Pain developed in the sciatic area, spreading thence over the whole body, with pain on deep pressure over the legs. Early in November, the left foot dragged in walking. She grew steadily worse. The right leg gave out, and difficulty in walking increased. She was slightly ataxic. On November 8, the hands became weak, with a general subsidence of pain. On November 10, she noticed diplopia for the first time. On the following day, a double facial paralysis appeared, with much pain over the mastoids, which was neuralgic and sharply localized. There were no general headache, vertigo or vomiting.

Examination.—The pupils were equal in size and regular in outline, with a normal light and accommodative response; the fields were normal by finger test; the fundi were normal, and there was no nystagmus; hearing was normal, with a positive Rinne test. There were considerable paresis of the left external rectus and slight paresis of the right external rectus, anesthesia in the distribution of the lower branches of the right fifth nerve, and a double facial paresis, greater on the right than on the left. The tongue, somewhat fissured, protruded to the left; the throat was normal, and the teeth were in fair condition. The arm reflexes were lost at the elbow and at the wrist, but the biceps reflex was retained on both sides. There was no ataxia. Over the ulnar distribution on both sides there was blunting to contact and pain and reduced reaction to temperature. There was pain on deep pressure over the right median and musculospiral nerves in both arms. Motion of the arms was normal, with a fairly firm hand grasp. The abdominal reflex was absent on the right and present on the left; the sphincters were uninvolved. The leg reflexes were unequal; the knee jerk was lost on the right and slight on the left. There was no achilles jerk, ankle clonus or Babinski sign, and only a very slight plantar response. Sensation was definitely blunted in the feet to contact, pain and temperature. There was also loss of position sense. The heart was normal; the pulse rate, 84; the blood pressure, 150 systolic and 100 diastolic.

Course.—Three days later, except for an increase in the paresis of the right leg, slow improvement began. In January, the patient was without pain, the diplopia had disappeared, and the facial paresis was growing less. Electrical examination

at this time showed no response to faradism. By February 1, she was essentially well, except for the persistence of definite facial weakness. During the remainder of the winter she had some return of pain and difficulty in speech owing to the facial weakness. The facial nerves at this time showed a reaction of degeneration. She had lost 23 pounds (10.4 Kg.).

Comment.—This case showed a typical onset, with moderate fever, followed after apparent recovery by pain, difficulty in walking, sensitiveness of nerve trunks and involvement of various cranial nerves, with definite diplopia for a time due to paresis of both external rectus muscles. There were also some disturbance of sensation in the right fifth nerve and a pronounced facial diplegia. With the exception of a slight knee jerk on the left, the deep reflexes were lost. There were likewise definite objective disturbances of sensation in the extremities. Improvement was uninterrupted but slow. At the end of two months the patient was without pain, the diplopia had disappeared, and the facial paralysis had begun to disappear, but with persisting electrical alterations. This continued until recovery was practically complete with the exception of some facial weakness, which has persisted to the present time.

This case differs from others in this series in that cranial nerves other than the facial were involved; this has been noted frequently by other observers. The severity and persistence, however, of the facial involvement are noteworthy.

Case 2.—A man, aged 42, married, the father of one child by a second wife, had formerly been rather a heavy drinker and had, in general, led a somewhat irregular life. For five years past, however, he had been working as a designer and had taken no alcohol. He is said by his physician to have had a low blood pressure which of late had returned to normal. On Dec. 4, 1928, he gave the following history: On November 30, he had eaten cold broiled lobster, but without immediate resulting symptoms of any sort. On December 4, however, he was obliged to go to bed with chilly sensations and a feeling of "soreness," but without fever. Pain developed at the back of the neck, extending over the right shoulder; it was rather dull. The patient was able, however, to go to a distant city on business under the supposition that he had merely a cold or slight influenza. On the next morning he was able to transact a certain amount of business. On the following day he remained indoors and took an occasional drink of whisky, amounting in all to about ⅔ pint up to the time when he returned home, a distance of perhaps 225 miles. That evening he remarked that "his legs didn't work right" and that his hands "tingled." He walked with an ataxic gait. As he thought that the disorder might be infantile paralysis, he was examined by a physician, an expert in the diagnosis of that disease, who found that he had no plantar reflex on the right, a slight one on the left, no Babinski response or Kernig sign, no triceps reflex and slight biceps reaction; that the pupils were normal, and that there was no Romberg sign in spite of an ataxic gait. Objectively, sensation was normal. The Wassermann reaction of the blood was negative. The white cell count and the differential count in the blood were normal. The urine showed no albumin or sugar. The heart, lungs and abdomen were normal; the abdominal reflex was first normal, but later disappeared.

Physical Examination.—On December 14, the pupils were much contracted, presumably from morphine; the reaction to light was slight; the accommodative response was normal; the visual fields were normal by rough test, and there was no nystagmus; the fundi were not examined. Hearing was normal, with the Rinne test positive; other cranial nerves were free except for a well marked paresis of both seventh nerves and a possible slight paresis of the soft palate. The tongue was coated; the throat showed large tonsils; the teeth were well cared for. The arm reflexes were absent at the elbow, wrist and biceps; there was some ataxia in the finger-to-nose test. The patient had considerable subjective tingling; objectively, the sensibility of the arms was normal to prick and contact. There was considerable pain on deep pressure over the nerve trunks on the left. The muscles were weak; the strength as indicated by the dynamometer was 25 on the right, and 20 on the left, about one fourth of the normal strength. The leg reflexes were the same on the two sides, with no knee jerks, achilles response, clonus or Babinski sign and possibly an extremely slight plantar reflex. Over the legs and feet there was marked loss of sense of contact (camel's hair brush) and considerable disturbance in the sense of position. The point and head of a pin were often not distinguished. There was considerable tenderness on deep pressure over the nerves of the legs; the sense of position of the toes was definitely disturbed, as was the vibration sense in both the legs and the arms; movements of the legs were extremely weak. The heart was normal; the pulse rate was 92, regular; the blood pressure was 130 systolic and 100 diastolic. The abdominal reflexes were absent. The liver was not enlarged, and the abdominal organs were normal; the sphincters were not involved.

Course.—A report from the attending physician stated that immediately after the examination reported an almost complete paralysis of respiration developed. Breathing was entirely diaphragmatic. The difficulty in breathing lasted about four and a half hours. Thereafter the patient began rather rapidly to recover, improvement starting in the face and extending downward.

At the end of six weeks the patient was able to return to work. He still had some weakness of the legs. In spite of business complications of a serious sort, he remained normal emotionally, rather more so than he had been previous to the illness. Outdoor work led to further decided improvement. He was active in all movements, but was considerably slowed down in speech and continued to have tingling sensations in the finger-tips at times. Aside from this, recovery has been complete.

Comment.—In this case there was no definite history of fever at the onset, but the patient was supposed to have had a cold or "slight influenza." The first definite symptom was weakness of the legs and tingling of one hand. Poliomyelitis was suspected. He rapidly developed paresis of both facial nerves, extreme muscular weakness, pain on pressure over the nerve trunks, absence of deep reflexes and some objective disturbance of sensation. Following a period of extreme difficulty in respiration, he began to recover, and in about six weeks was back at work with, however, some persisting weakness in the legs and slight subjective disturbance of sensation. Otherwise, recovery was complete.

This case corresponds closely to the type with practically uncomplicated neuritic symptoms and double facial paralysis. A preceding

febrile attack is probable, but could not be definitely determined. The interval between an apparently insignificant respiratory infection and the onset of paralytic symptoms is noteworthy and somewhat characteristic.

Case 3.—An unmarried woman, aged 60, was first seen by Dr. H. R. Viets, through whose courtesy this report is made, on Sept. 14, 1929. She had been operated on for appendicitis, had had an attack of pyelitis three years before and for a time had had colitis. She had had no difficulty with the tonsils or sinuses and had had no infectious disease during the preceding summer, although she was somewhat affected by the hot weather. During the following winter, she had been well up to two weeks before the onset of the present illness, when as a result of a fall she injured her knee; this, however, appeared to be a matter of small consequence. A week after the injury, she began to have general pain and insomnia. No fever was noted at any time. On the morning of September 14, a left facial paresis developed. She was then having severe pain in the back and in the right hip and leg, with uncomfortable nights. The bowels were slightly sluggish; micturition was normal. She had been able to walk until September 13. The blood pressure was 140 systolic; the heart was normal; the pulse rate was 68.

Physical Examination.—There was marked swaying in the Romberg position; the pupils were normal; accommodation was normal; there was no nystagmus; the fundi were normal. There was definite left facial paresis, involving all branches; the other cranial nerves were not involved, except possibly for some difficulty in swallowing. The arm reflexes were equal and active; there was no ataxia; motion was normal; the hand grasps were strong. There was no objective disorder of sensation in the arms, but there was some subjective complaint in the form of paresthesias. The leg reflexes were lost on the right and slight on the left; there were no achilles reflexes, ankle clonus, plantar reflex or Babinski response. The muscles were generally weak, but there was no actual paralysis and no definite tenderness over the nerve trunks. There was paresthesia of the legs, "pins and needles." There was no tremor; speech was normal.

Course.—Between September 14 and 17, there had been a considerable decrease in the amount of pain. On September 16, the right side of the face had become involved, and there was increasing weakness of the legs so that neither could be moved on September 17. The left arm also was almost completely paralyzed; the right somewhat less. For some hours there had been increasing difficulty in breathing. At the time of the examination, the respiratory rate was 35, and the patient was breathing in short gasps. She was able to talk, but with difficulty owing to the shortness of breath. The face and finger-tips were cyanotic, with profuse sweating. The legs were completely paralyzed; the abdomen was distended and tympanitic; there was respiratory failure. The patient died on the same day. No necropsy was performed.

Comment.—There was no adequate etiology in this case, and no rise of temperature was noted at any time. Following general pain, unilateral facial paresis developed, followed shortly by paresis of the other seventh nerve. There was no definite involvement of other cranial nerves beyond some slight difficulty in swallowing. The patient had subjective disturbance of sensation, with practical loss of the deep leg reflexes, rapid progress of the paralysis, later involving the arms,

increased difficulty in breathing, cyanosis and death three days after the acute onset of symptoms.

The case is noteworthy for its extremely rapid course, apparent absence of fever at any time and no period of latency.

CASE 4.—A physician, aged 51, unmarried, whose history previous to the present illness was uneventful, was a man of unusual regularity of life, an active practitioner in a special field. He neither smoked nor used alcohol, and had been fond of athletic exercises, keeping himself thereby in excellent condition. Early in September, 1929, he had a tooth removed; it was a somewhat difficult procedure. He was more or less ill for several days, apparently in consequence, and suffered from diarrhea. At this time he had generalized pain. In the latter part of November, he ate something that apparently set up more or less gastro-intestinal disturbance; he was nauseated but did not vomit. He also had further trouble with his teeth.

On December 6, the patient began to have pain in the right shoulder, and on December 12 complained of excessive soreness over the whole body. On the next day, he had difficulty in defecation and micturition and dull pain in the legs, and he was extremely drowsy, with increasing "soreness," particularly in the legs. In the days immediately following, he had further pain in the shoulder, severe enough to require morphine. On this date a slight paresis of the left side of the face developed, with inability to close the left eye properly and with some drooping of the left side of the mouth. The pain became more severe and was cramplike, involving also the right thigh. The pain tended to increase and to extend. On December 16, he was not able to move the legs freely; the left ankle was slightly swollen; the pain was somewhat less; there was some sphincter disturbance, with continued soreness in the legs and arms. Two days after the appearance of the left facial paresis, there appeared a right paresis of pronounced character, so that for several days he had a fairly complete facial diplegia; he, however, improved rapidly, and at the end of a week from the onset had essentially recovered. He had, however, increasing pain in the left shoulder and leg, with occasional cramps in the muscles; feelings of numbness and greater weakness developed in the legs; they could be raised from the bed only with much difficulty.

Physical Examination.—The patient was first seen by one of us (Dr. Taylor) on Dec. 14, 1929. The observations made were: The pupils were equal, circular and of moderate size, with a normal reaction to light and in accommodation; the visual fields and ocular fundi were normal; there was no nystagmus; hearing was unimpaired, the Rinne test was positive. Except for a well defined paralysis of the left facial nerve, the cranial nerves were normal. The arms showed no reflexes at the elbow, wrist or biceps. There was no ataxia; motility was unimpaired. There was some pain, not pronounced, on pressure over the median nerve and over the muscles in general; strength by the dynamometer was 50 on the right and 40 on the left. The knee jerks were lost; there was no achilles response, and no clonus or Babinski sign; there was an exceedingly slight, barely demonstrable plantar response. Sensation in the legs was objectively normal. There was at this time no paralysis; position sense was normal. There was pain over the right thigh on deep pressure, and also in the calves, but the patient thought that this was less than before; there were no tremors; speech was normal; the tongue was somewhat coated; the throat was normal; the teeth were in fair condition, one or two being devitalized; one had recently been extracted. The heart was normal; the pulse rate was 80, and the rhythm regular; the blood pressure was 110 systolic and 70

diastolic. The abdominal reflexes were absent. The abdomen showed no distention. The sphincters were not involved. The patient was perfectly clear mentally.

Course.—A subsequent examination, on December 19, showed a fairly complete paralysis of both seventh nerves. The left facial paresis at this time had, however, begun to improve somewhat. The muscles, in general, were decidedly weak, but there was no complete paralysis. On January 3, improvement was very pronounced; the facial muscles had practically recovered; the patient was able to close the eyes adequately and to make various movements with the mouth muscles; the strength of the right leg had markedly improved, and he was able to stand alone. Thereafter, he improved to such an extent that he was able to go away for three weeks, but, as noted, he continued to have pain in the legs, especially on pressure. There was also tingling in the finger-tips.

On February 18, strength as shown by the dynamometer had greatly improved. The abdominal reflexes had returned on the left. No plantar or other reflexes were obtained at this time. The patient was able to walk perfectly well. There was a little tremor of the right hand, at times rather coarse in character, and possibly slight blunting of sensation to prick, but contact and temperature were perfectly appreciated. A pronounced paralysis of the right serratus magnus had developed. Electrical examination of the flexor forearm muscles (right arm tested) showed a quick response to both faradism and galvanism; there was, however, a suggestion of slowing of contraction to the galvanic current in the thenar muscles; the facial muscles responded normally—cathodal closure contraction was greater than anodal closure contraction.

On April 3, disturbance of sensation could be demonstrated objectively on the inner side of the left thumb and over the dorsal median side of the wrist. The index finger and thumb felt numb and were painful. In general, strength had returned, but movements were somewhat restricted on account of pain. The outer side of both knees was somewhat painful on pressure. The paresis of the serratus magnus had shown no improvement. The facial nerves were entirely normal. In spite of a persisting fine tremor of the right hand, the patient was able to do a cataract operation satisfactorily, although he was somewhat handicapped by the serratus paralysis. There still remained some subjective disturbance of sensation in the feet and in one arm. On November 22, the improvement was pronounced. The chief complaint then was a practically universal "soreness" of the muscles; the serratus palsy had improved. In a small area of the inner side of the thumb of the left hand there was still an area of subjective numbness and objective disturbance both to contact and to pinprick. The facial nerves had completely recovered; the knee jerks were still lost, but a definite achilles jerk was easily obtained. There were also normal reflexes over both the triceps and the biceps tendons, which had been lacking at the previous examination. The wrist reflexes were not obtained. In general, the condition was excellent and amounted to a practical recovery, although the patient felt that in some respects he was not back to a normal condition. Since then, he has improved still more, so that now only the slightest residual of disturbed sensation remains.

Comment.—Apart from the removal of a tooth and a gastrointestinal disturbance, with some generalized pain about a month before the onset of the acute symptoms, there were no significant prodromes. The patient was absolutely sure that there had been no rise in temperature at any time. The first symptom, pain in the right shoulder, was followed in a week by excessive soreness over the whole body. Tempo-

rary difficulty with the sphincters occurred; there was a dull pain in the legs, extreme drowsiness, increasing soreness and slight paresis of the left side of the face. Pain was extremely severe, requiring morphine. There ensued increasing weakness of the legs, temporary sphincter paralysis, extension of the facial paralysis to the right side and a serratus paralysis. Within two weeks, improvement began and was uninterrupted. Recovery was essentially complete except for some persisting soreness of the muscles and slight disturbance of sensation.

It is noteworthy that the facial paralysis was early in appearance, that there was a long persisting serratus paralysis, and that there was no antecedent history of fever.

CASE 5.—A Scotchman, aged 20, born in the United States, a worker in a lunchroom, married, a hardworking energetic man of athletic type, was admitted to the neurologic clinic of the Massachusetts General Hospital on Nov. 26, 1930. He had had no previous illness of note. Three weeks preceding admission, he had had numbness and weakness in the hands and feet and was suffering from a slight cold. A week later, weakness developed in the legs and rapidly progressed to almost complete paralysis. During the first few days, while the paralysis was coming on, he walked unsteadily and fell once. Disturbance of sensation in the fingers steadily increased until, as he expressed it, "they came to feel as if asleep." There was also some generalized aching pain in the body. Three or four days before admission, the mouth became dry and parched, in spite of excessive drinking of water, with accompanying indistinctness of speech. Three days before entrance, the eyes frequently "rolled up" and continued to do so. There was at this time very slight sphincteric disturbance, and occasional vomiting, not of the projectile type. On one occasion he had tinnitus, and on one day headache. No rise in temperature was noted.

Examination.—When the patient entered the hospital, he had an appearance of definite illness. Breathing was somewhat irregular and slightly labored—largely diaphragmatic. The eyelids were half opened, the neck was stiff, and there was a bilateral Kernig sign. He was able to move the feet and legs slightly; the hands were weak, the arms somewhat less so. There was no atrophy, tremor or fibrillation, and the muscle tone was normal. The gag reflex was active; the corneal reflex was present; no biceps, triceps or radial response was elicited on either side; no abdominal or cremasteric reflex was obtained; the knee jerks were lost; there was no clonus or Babinski sign; the jaw jerk was present; sensation to pinprick, contact and heat and cold was normal; there was tenderness on deep pressure over the muscles of the legs; position sense was disturbed in the toes and hands; the cranial nerves were normal, except that both seventh nerves showed generalized weakness, equally on the two sides; speech was slightly affected, presumably on account of the facial paresis. A slight left external strabismus was noted on looking toward the right. Apart from the nervous system, examination gave negative results. The patient's memory of the present illness was inaccurate.

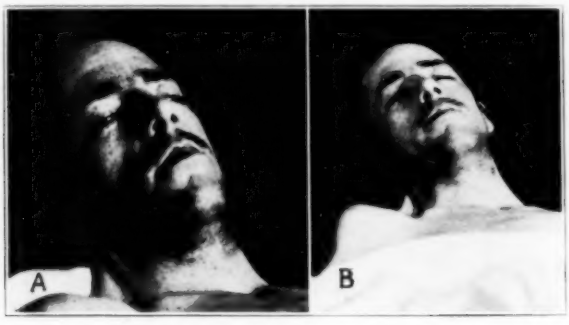
Laboratory Examinations.—On November 27, the blood showed: 4,950,000 red cells; 9,000 white cells; hemoglobin, 85 per cent; red cells and platelets, normal; polymorphonuclear cells, 70; lymphocytes, 24; large mononuclears, 4; eosinophils, 0; basophils, 0, and transitional cells, 1.

A lumbar puncture gave clear fluid, which was slightly xanthochromic; the initial pressure was 190; jugular compression gave normal results; the fluid contained: 4 lymphocytes; the total protein was 206 mg.; the sugar, 67 mg.; the Wassermann reaction was negative; a pellicle was present.

A cisternal puncture made on December 1 also gave a clear but colorless fluid. The cistern was drained; the fluid showed: normal dynamics; 2 lymphocytes, total protein, 49 mg.; colloidal gold curve, 1111110000; sugar, 70 mg.; chlorides, 722 mg.; Hinton test, negative; Wassermann reaction, negative.

Course.—In the hospital the patient steadily improved. On December 6, he had a slight chill, with moderate sweating, pain in the abdomen, slight pain in the extremities and a temperature of 99.6 F.; the pulse rate was 110; the respiratory rate, 20; the lungs were clear; there was no urinary disturbance; the abdomen was distended; he complained of pain in the abdomen and lower part of the chest; the urine showed no abnormality.

By Jan. 5, 1931, except for a certain amount of general weakness, the patient had practically recovered. There still remained a very slight feeling of numbness at the finger-tips, and the face showed a slight lack of mobility.



Patient in case 5, showing facial paresis. *A*, attempt to close the eyes. *B*, one week later; marked improvement.

A detailed physical examination made on January 5 showed the pupils to be rather large, equal and regular in outline, with an excellent reaction to light and in accommodation; the fields were normal by rough tests; there were slight nystagmoid movements on extreme lateral fixation, but within normal limits. The fundi showed normal disks, but with extremely blurred edges on both the temporal and the nasal sides. The Rinne test was positive. The other cranial nerves were free, with the exception of slight bilateral facial weakness. The tongue was normal and protruded in the median line; the throat was normal, with a retained gag reflex; the teeth were in good condition. The arm reflexes were not obtained at the elbow, wrist or over the biceps tendon. There was no ataxia; motility was unimpaired. Sensation was objectively normal. The strength, measured by the dynamometer, was 60 on the right and very slightly less on the left. The knee and achilles jerks were not obtained; there was no clonus, and the plantar reflexes were normal. Sensation in the legs was normal; position and vibration sense were normal; strength was good and rapidly improving. The patient had been able to stand but had not as yet walked. There were no tremors. Speech was normal. There was still considerable pain on deep pressure over the whole length of the

sciatic nerves. The liver was not enlarged, and the abdominal organs in general were normal. The sphincters were entirely controlled. The abdominal reflexes were present. The heart sounds were normal; the pulse rate was 104, the rhythm regular; the blood pressure was 125 systolic and 80 diastolic.

Mentally, the patient was alert and anxious to leave the hospital. He was evidently on the way to complete recovery.

Comment.—There was probably a slight infection a week before the onset, but without a known rise in temperature. The chief symptoms were: weakness of the legs, progressing to almost complete paralysis, subjective disturbance of sensation in the extremities, general pain, some sphincteric disturbance, occasional vomiting, later affection of the arms, double facial paralysis, absence of deep reflexes and tenderness on deep pressure over the muscles of the legs. Rapid improvement followed. Within six weeks, there was practical recovery, with some slight persisting weakness in the body muscles and face.

This case is typical of the general symptom complex and presents nothing unusual. The observations on spinal fluid are of particular interest in respect to the disparity between the total protein in the lumbar and the cisternal fluid.

CASE 6.—A carpenter, aged 57, who had had a fall of 15 feet in 1912, the details of which are not known, had been able to work for three years thereafter, but a year before being examined, on Oct. 31, 1916, he began to have weakness of the legs without rigidity and without pain.

Examination.—There was no disturbance of sensation; the hands and arms were unaffected, and the sphincters were controlled. The left pupil was slightly larger than the right, and the reaction to light was limited. The knee and achilles jerks were absent. There was some hypotonia. The Wassermann reaction of both the blood and the spinal fluid was negative; the fluid contained only 1 cell. The total protein was not estimated.

Course.—On December 11, the following change were noted: The pupils were irregular and reacted slugglishly to light, but well in accommodation; there was no paralysis of the ocular nerves; there was no diplopia or nystagmus; the Rinne test was positive. There was paresis of both seventh nerves leading to imperfect facial movements and difficulty in smiling; there was considerable tremor about the mouth; the fifth nerve was not involved; there was no palatal paralysis; the condition of the teeth was poor; the tongue was roughened, but with normal movements, although atrophic in appearance and somewhat tremulous. The wrist and elbow reflexes were absent; there was no pain over the nerve trunks; there was slight ataxia in the finger-to-nose test; the strength as measured by the dynamometer was 20 in each hand; the systolic blood pressure was 150. The abdominal reflexes were normal, but there was no cremasteric response; there was no atrophy of the muscles; no pain over the sciatic nerves on pressure, clonus, Babinski sign, achilles jerk or disturbance in sense of position; there were some fibrillary tremors over the back and neck; there was fair strength in the legs.

On Jan. 25, 1917, the condition was essentially unchanged; a myasthenic reaction was not demonstrated; there was no lead in the urine; considerable tremor was present about the mouth, especially on the right side. Electrical examination of the seventh nerve gave no contraction, either direct or indirect, to strong faradic

currents; there was no pronounced reaction to galvanism, excepting over the lower facial muscles, where there was a quick response; the responses in general were less on the right than on the left.

Nearly a year later, the patient thought that he was still growing weaker.

Comment.—The onset occurred with weakness of the legs, without pain. There was loss of the knee and achilles jerks, with some hypotonia. There was no paralysis of the ocular nerves, but paresis of both seventh nerves was present; there was no pain over the nerve trunks or muscular atrophy. The myasthenic reaction was negative; there was increasing muscular weakness. Beyond general failure in strength and lost reflexes this patient had no definite evidences of neuritis.

In spite of the definite, though not particularly pronounced, paresis of both seventh nerves, this case presumably is to be included in the general category under discussion on account of the combination of facial paralysis, muscular weakness and loss of deep reflexes, but is otherwise atypical.

CASE 7.—A factory worker, aged 29, unmarried, on March 30, 1917, said that he had had weakness of the right leg with pain in the knee for four weeks, double vision for six weeks, left ocular ptosis for three weeks and weakness in both arms for four weeks.

Examination.—There was ptosis of the left eyelid; the pupils were active to light and regular in outline; the throat was normal; the heart and lungs were normal. The arm reflexes were normal; the left knee jerk was present, the right absent; there was no clonus, Babinski sign or Romberg sign. On lateral fixation in either direction, nystagmoid movements developed. The right external rectus was weak and all movements of the eyes were somewhat limited. The left superior and inferior rectus muscles were weaker than the right. The ocular fundi were normal.

Course.—On April 5, there was paresis of the third, fourth and sixth nerves, with normal disks.

On April 24, the patient had been having difficulty in talking for some days; this was worse in the afternoons and evenings; facial weakness also had developed.

On May 1, there was definite ptosis of the right lid and facial diplegia. The patient was in the hospital for about a week, and was discharged with a diagnosis of "double external ophthalmoplegia with facial diplegia."

On May 16, the patient was having considerable difficulty with speech because of the facial paralysis. The right side of the forehead wrinkled less than the left; ptosis persisted, being less on the left than on the right. Ocular movements to both sides had somewhat improved. For the past two days, the fingers of the right hand had seemed weaker; he was unable to button his collar; both knee jerks were present, the left being greater than the right. (The patient is said to have had poliomyelitis as a child and a "shock" four years before examination.) The biceps jerks were normal and active; there was no Babinski or Romberg sign; faradic stimulation of the arm flexors showed no unusual tiring.

On January 21, there had been no definite improvement.

Comment.—The onset was with weakness of the right leg and pain about the knee, together with weakness in both arms. There had been diplopia for six weeks, nystagmus on lateral fixation and weakness of

the recti muscles; later, facial paresis developed and still later, ptosis of the right lid and definite facial diplegia were present. A diagnosis of double external ophthalmoplegia with facial diplegia was made, ignoring the general muscular weakness.

This case also is perhaps doubtful of classification. The combination of definite weakness in the extremities with double facial paralysis is suggestive, although several of the cranial nerves were involved as well. It may be regarded as a possible transitional case.

CASE 8.—A woman, aged 42, married, who was examined at the Massachusetts General Hospital on April 12, 1921, had had facial paralysis with numbness of the legs for three months. Eight years before, she had had an acute attack of tonsillitis. Shortly afterward, she had noted an inability to move the left wrist. Four years previously, she had a second attack of tonsillitis. One year prior to admission, there was inability to move the left shoulder for a week. Six months previously, weakness of both thighs developed. Five and a half months before admission, she had abdominal pain and immediately afterward pain radiating down both legs; at the same time she noticed immobility of the face and thick speech. The legs felt numb. She later had a third attack of tonsillitis, but for the four months preceding examination at the hospital had gradually improved.

Examination.—The patient was able to walk; her speech was more normal; facial paralysis, however, persisted. The pupils reacted to light, and there was no nystagmus. Facial paresis was more marked on the right; the biceps reflexes were present, the knee jerks absent and the achilles jerks present; there was no Babinski sign, and no actual Romberg sign, but some unsteadiness. A report from the Eye and Ear Infirmary stated that there was blurring of the nerve heads on the nasal margins. In general, the patient had improved and was annoyed chiefly by the inability completely to close the eyelids.

Comment.—For three months, the patient had had facial paralysis with numbness of the legs. In the past she had had a temporary paralysis about the left shoulder, more recently paresis of both thighs. Later, there was pain radiating down both legs with immobility of the face. She had gradually improved, with persisting facial paresis which was somewhat more marked on the right. The knee jerks were absent.

This case presents a very subacute onset with final involvement of both facial nerves and somewhat generalized motor weakness and vague sensory disturbance. This may also be regarded possibly as an abortive case, of a chronic character, of the general syndrome. The association with repeated attacks of tonsillitis is perhaps suggestive.

CASE 9.—A mill worker, aged 22, unmarried, who was examined on March 3, 1925, had never had any significant illness, accident or nervous disturbance. He lived in a rooming house and ate in restaurants. He was somewhat alcoholic. So far as known, he had had no venereal disease. About three weeks before examination he had had a cold and a mild sore throat, but was able to continue at work. On February 27, he noticed that his legs were weak when dancing and also when at work. On the following day, he had difficulty in micturition, necessitating catheterization.

Examination.—The legs were objectively weak, and the reflexes were lost. The deep muscle sense was poor, and the calf muscles were tender. The arms were also weak, especially at the wrist; this, however, the patient had not himself noticed. The elbow jerks were absent. There was no atrophy and no tremor. In addition, there was a bilateral facial paralysis. Station was somewhat uncertain. He stated that in the mornings he could not swallow or talk well until he had been awake for a few hours. Mentally, he was clear. The Wassermann reaction was negative. There were 6 cells in the spinal fluid, and a slight trace of globulin and albumin. The urine was without albumin or sugar.

Course.—The patient began to improve almost at once. On March 18, he was able to walk about the house and could stand alone. He had no further difficulty in micturition, and had no complaints except the continued weakness of the legs and the facial paralysis. The muscles of the legs were reduced in tone but were not tender. The reflexes had not returned. On April 10, he could go up a flight of stairs without help other than the banister. He was at this time able to close his eyes, but the facial paralysis was still apparent. He was not seen again.

Comment.—Following a sore throat, the legs became weak and there were sphincter disturbance, loss of reflexes, tenderness on pressure over the muscles and bilateral facial paralysis. The spinal fluid was not remarkable. Rapid improvement took place, with continued loss of reflexes and persistent facial paralysis.

This case conforms closely to the type with definite polyneuritic symptoms and signs, and pronounced facial paralysis. It is noteworthy that three weeks previous to the onset the patient had had a mild infection of the upper respiratory tract.

CASE 10.—A boy, aged 18, was admitted to the Rhode Island Hospital on Feb. 2, 1931, complaining chiefly of progressive weakness of the legs for nine days. He had contracted chickenpox from a younger brother two weeks before and had been confined to the house. He was, however, not particularly ill and was able to be about and occasionally to go outdoors. He had received no medication. On January 24, he had noticed weakness of the legs when he got up in the morning. The weakness increased on the following day, and he had a slight headache and felt drowsy. He did not improve and began to notice difficulty in swallowing, some disturbance in speech, transient diplopia and slight blurring of vision. He also had some difficulty in micturition. The day before admission, the legs had become so weak that he could not stand. There was nothing of importance in the family history. He had had measles, mumps, whooping cough and infrequent colds, but never had been seriously ill before. There was no history of an accident. He had been brought up on a farm, reaching the eighth grade at school, and then went to work in a mill. He lived at home and did not use tobacco, alcohol or drugs in any form.

Physical Examination (by Dr. McDonald).—The patient was mentally clear. Speech was thick and had a nasal twang. He did not use the lips in speaking, and the face was masklike. He made few voluntary movements. The pupils were moderately dilated, circular, the left larger than the right, and reacted normally to light and in accommodation. There was no strabismus. He had, however, a horizontal nystagmus. There was definite bilateral facial paralysis; otherwise, the cranial nerves were normal. There was pronounced weakness of the arms, and the legs were almost completely paralyzed, with tenderness of the thighs and

calves. The superficial reflexes were normal, excepting that the upper abdominals were not obtained. The corneal reflex was present, but the biceps, triceps, knee and achilles jerks, Babinski, Oppenheim, Gordon and Chaddock signs were all absent. The sphincters at this time were normal, and there was no vasomotor disturbance. Apart from the defects noted, examination gave negative results, including urinalysis. Fluid from a lumbar puncture showed 3 lymphocytes, negative Wassermann and Hinton reactions, a total protein of 171 mg., a trace of globulin, normal sugar, an initial pressure of 170, which rose to 230 after jugular compression, equally on the two sides; after the removal of 10 cc. of fluid, the final pressure was 110. The colloidal gold curve was 1223432100.

Course.—On February 6, tenderness of the thighs and calves still persisted, but the patient was able to move the legs somewhat. On February 9, there was marked improvement in the movements of the legs, and the facial movements were beginning to return.

Comment.—Following chickenpox there developed weakness of the legs, with slight headache, difficulty in swallowing, disturbance in speech, transient diplopia, slight involvement of the sphincters and double facial paresis; the legs were almost completely paralyzed, with tenderness on pressure, and the deep reflexes were lost. Slight changes were present in the spinal fluid, with a colloidal gold curve in the syphilitic zone. Improvement began within a week after the onset.

This case is noteworthy from the fact that cranial nerves other than the facial were somewhat involved. The symptoms in general are entirely characteristic of the syndrome under consideration. Globulin was present to a slight degree, but there was an increased total protein, with a cell-albumin dissociation.

CASE 11.—A girl, aged 7, who on Jan. 27, 1919, had complained of weakness of the legs, six weeks before had had "influenza," but recovered and returned to school. Two weeks before the onset, the legs were more or less painful, but she was able to go about for a week. At the end of that time, however, she limped so badly that she could no longer leave the house. Birth had been normal. She had walked and talked at the proper time. She was a large child and had bow legs. She had had many of the children's diseases, among them diphtheria.

Physical Examination.—There was no difficulty in swallowing or talking; the ocular fundi were normal; the eyes closed weakly, and there were no nasolabial lines; there was double facial paresis of moderate degree. The arms and legs were symmetrically weak; tendon reflexes were absent, and there were toe-drop, foot-drop and tenderness of the nerve trunks. She swayed in the Romberg position. The muscles of the neck and back were weak. She had some pain in the back. The family history was unimportant.

Course.—The patient showed gradual improvement during a number of months. She was last seen on Sept. 5, 1919, and was then well. The deep reflexes had returned, and the facial expression was normal.

Comment.—The onset of weakness of the legs and pain followed an attack of "influenza" six weeks before. There were moderate double facial paresis, absence of deep reflexes, gradual improvement and final

complete recovery at the end of about seven months with a return of the deep reflexes and disappearance of the facial paralysis.

This case is characteristic and without complications. In this instance, also, the onset was preceded by a respiratory disturbance.

CASE 12.—A man, who was admitted to the Massachusetts General Hospital on Dec. 27, 1928, had suffered from general progressive weakness for three and a half weeks. At the onset there was numbness of the hands without pain, followed by the same feeling of numbness in the calves of both legs, but he was able to continue work. Ten days later, he was incapacitated by marked weakness of both arms and legs. In 1924, he had been in a Government Hospital for eighteen days for some difficulty with an ear, the exact nature of which was not determined. Three examinations of the blood had given negative results.

The patient had had photophobia five months before, without headache or vertigo. For a brief period he had had a cough with a whitish sputum, but without chills or fever. He had had a few night sweats; there were no cardiac symptoms. Appetite was good; the bowels were regular, and there was some nocturia.

Examination.—The patient was fairly well developed and nourished; when seen in the hospital, he did not appear acutely ill. There was a questionable slight ptosis of the left lid; the sclerae were clear; the pupils were somewhat oval in outline, but were regular and reacted to light and distance. The ears and nose were normal; there was slight drooping at the right angle of the mouth; the teeth were in poor condition; the pharynx was normal; the tongue protruded in the midline; there was no adenopathy. The chest was resonant; the breath sounds were vesicular; there were no râles; the heart was not enlarged, the sounds were normal and without murmurs; the blood pressure was 130 systolic and 90 diastolic; the liver and spleen were not palpable; there was no tenderness or masses in the abdomen; there was no edema. There were a marked loss of power in the arms and legs, which was more on the extensor side, and a slight wrist-drop; joint and muscle sensation was normal; there was a dulness of sensory perception, which extended from the feet to the lower part of the abdomen and from the hands to the elbows. There was some pain on pressure over both calves, and over the biceps and triceps. The biceps and triceps reflexes were not obtained; the abdominal reflexes were present; the knee jerks were lost; there was no Babinski response. Roentgenograms of the skull and spine showed no abnormalities. The patient was not able to walk.

A blood count on entrance showed: 17,000 white cells, with 84 per cent polymorphonuclears; later these figures were 13,000, and 78 per cent polymorphonuclears. The red cells numbered 5,020,000, with 80 per cent hemoglobin.

Course.—On Jan. 2, 1929, the weakness of the extremities had increased, with bilateral wrist-drop and ankle-drop. There was slight respiratory embarrassment. Roentgenograms of the sinuses and teeth showed evidence of thickening of the mucous membrane in the left maxillary, sphenoidal and ethmoidal region. Several teeth were carious, with infection at the root of the upper right bicuspid. The urine was normal.

On January 5, the patient had difficulty in swallowing and took liquids sparingly; there was considerable respiratory embarrassment. The general condition was poor; the temperature was normal, the pulse rate was 120, and the respiratory rate, 30. On the following day, oxygen was used; weakness was profound. Against advice the patient was taken home, where he died. No necropsy was made.

Comment.—This patient gave a history of progressive weakness, with numbness of the hands without pain. He was able to continue at work during the first weeks. Objectively, there were general muscular weakness and dulness of sensory perception in the arms and legs, with some pain on pressure over both calves and in the arms. There was loss of the deep reflexes.

This case is not characteristic in that no pronounced facial paralysis developed. The progressive loss of strength in the extremities, with sensory disturbance, suggests a polyneuritis. The progress of the disorder, with loss of deep reflexes, resulting in death, places it roughly in the vague category of so-called Landry's paralysis. In spite of the absence of pronounced facial paralysis, the case may be included in this series as an aberrant form of the symptom complex with merely a suggestion of facial involvement.

CASE 13.—A wire worker, aged 33, married, who was examined at the Massachusetts General Hospital on Dec. 14, 1918, complained of difficulty in swallowing and continual tinnitus. The family and past histories were of no importance. There had been no trauma or infections. He had had continual frontal and occipital headache for four days and vertigo for several days. Diplopia then developed, with blurring of vision, and mastication became difficult because of paralysis first of one side of the face and later of both.

Physical Examination.—The scalp, skin and ears were normal; the eyes reacted to light and in accommodation. There was a suggestion of choking of the disks on both sides, which was more pronounced on the left. The visual fields were normal; there was no diplopia; the ocular muscles were normal. There was paralysis of both facial nerves. The patient had difficulty in swallowing, but the throat reflexes were normal. There was no tremor of the tongue. The reflexes in general were normal and active, and no pain was present over the large nerve trunks. There was no Babinski response or clonus. The various paralyses were progressive. The blood pressure was 145 systolic and 100 diastolic; the pulse rate was 80; the temperature, when examined, was normal. The urine was normal, and there was no incontinence.

Comment.—For four days, this patient had continual frontal and occipital headache, vertigo, with diplopia, blurring of vision and difficulty in mastication, and paralysis of both facial nerves; the deep reflexes were normal.

Apart from the double facial paralysis, this case has few analogies to the type of disturbance here under consideration. The history available is insufficient to justify a definite diagnosis. The double facial paralysis is, however, suggestive.

CASE 14.—An American housewife, aged 40, who was admitted to the neurologic service of the Massachusetts General Hospital on March 24, 1931, for two weeks had had paresthesia of the hands, followed by pain in the left shoulder and upper arm, together with weakness of that arm. Later, the right upper arm was similarly affected. There was also paresthesia of the feet, followed by numbness and complete paralysis, with some diffuse pain in the calf muscles. A week before

entrance, she had difficulty in swallowing and weakness of the facial muscles. On admission, all these symptoms had improved, but there was pronounced paresis both of the face and of the extremities. Catheterization had been necessary on the day before admission. There was no history of the ingestion of alcohol, Jamaica ginger, lead, arsenic or other drugs as possible causative factors. The family and marital histories were unimportant.

Physical Examination.—Apart from the nervous system, the results were negative. On entrance, the patient was apathetic and restless but mentally clear. She showed a pronounced bilateral facial paralysis, greater on the right than on the left. There was some difficulty in swallowing, but less than it had been at first. The other cranial nerves were free. Sensation of all types was diminished over the legs, with a pronounced disturbance in position sense. Sensation to pinprick was diminished in the arms and hands. The corneal and gag reflexes were normal; the biceps, triceps, radial, abdominal, knee and achilles reflexes were absent; no Babinski sign was present. There was marked weakness of all muscle groups, greater in the lower extremities. She had no control over the feet, legs or thighs, except that the feet could be moved slightly. She was unable to sit up unsupported. The arms were also extremely weak, with general loss of muscle tone, but without fibrillation, and there was pain on pressure over muscle groups, especially in the legs. The urine was normal. A differential blood count showed no abnormality. Lumbar puncture gave a clear, slightly xanthochromic fluid with an initial pressure of 95; the dynamics were not remarkable; the fluid contained: 2 lymphocytes; globulin, +; alcohol, +++; total protein, 336 mg., and sugar, 73.5 mg.; the colloidal gold curve was 2334444443; the Wassermann reaction was negative.

Course.—On March 30, there was decided improvement. Except for the following facts, examination of the nervous system gave negative results. There was still slight weakness about the lower facial muscles, but the eyelids could be closed with good strength. There was slight fibrillation in the upper lip; the movements of the right arm were fairly complete; the left arm was still decidedly weak in all movements; strength as registered by the dynamometer was: right, 10; left, less than 5. There was some pain on pressure over the nerves of the arms, particularly on the left; the abdominal reflexes, arm reflexes, knee and achilles jerks were absent; there was no ankle clonus or Babinski sign. There was considerable tenderness on pressure over the nerves and in the calves, the left leg being more affected than the right; there was pronounced loss of position sense in the great toes. Vibration sense was normal; there was no astereognosis. Paralysis of the face, which had been complete for only two or three days, showed rapid improvement from that time on.

When discharged, the patient was practically well.

Comment.—The onset with general muscular weakness was followed by facial diplegia, slight sphincter disturbance, pain on pressure over the nerves and various objective sensory defects. The spinal fluid was slightly xanthochromic, with markedly increased total protein and 2 cells (albuminocytologic dissociation). Recovery was rapid, and was most pronounced in the face.

This case ran a characteristically typical course.

CASE 15.—A boy, aged 18, unmarried, who was admitted to the neurologic service of the Massachusetts General Hospital on April 29, 1930, two months before had had a temporary loss of appetite and complained that his hands and

fingers trembled. Later, this developed into definite weakness of the arms and hands. He tired easily and was able to walk only a short distance. Beyond supposed influenza and occasional colds in the head, he had had no illness immediately preceding the present illness, but he had lost some weight.

Physical Examination.—There was some blurring of the disk margins; the fields and visual acuity were normal; there was no nystagmus; the pupils were normal. There was paresis of both seventh nerves, without involvement of the other cranial nerves. The gait was ataxic; there was slight tremor of the intention type; the Romberg sign was positive. There was weakness of the hand grasp by the dynamometer; vibration sense was diminished, and there was loss of the sense of position. The deep reflexes were in general lost; the legs were weak, and movements of the feet were impaired. The patient was unable to sit up unaided on account of weakness of the abdominal muscles. When lying down, he was unable to raise the legs from the bed. There was slight diminution of pain sense in both hands and feet, with slowing of perception, but no tenderness over the nerve trunks. The disks at no time showed a definite choking. The interossei muscles became weak, and slight atrophy of the small muscles of the hands developed. Roentgenograms of the skull gave negative results. The temperature was normal during the patient's stay at the hospital, except for one day, when it reached 100.6 F.; the pulse rate was generally high, averaging 100, and at one time reached 128; respiration was normal.

A blood count was normal; urinalysis gave negative results. Numerous spinal punctures were done during less than a month while the patient stayed at the hospital. The fluid was clear, slightly xanthochromic, "sticky," with normal dynamics; it contained 15 lymphocytes; the total protein was 648 mg.; the magnesium sulphate precipitation was +++; the colloidal gold curve was 0112344443; the Wassermann and Hinton reactions were negative. Subsequent punctures showed similar but somewhat varying conditions; the total protein at one time reached 708 mg., and the cell count, 169 cells, with 6 mononuclears.

Course.—On Jan. 22, 1931, the right pupil was slightly larger than the left and was slightly irregular in outline; the response to light was present but slow; accommodation was normal; the visual fields were normal; there were slight nystagmoid movements on extreme lateral fixation, rather more marked on looking toward the right; the fundus veins were somewhat congested; the outlines of the disks were slightly blurred, but there was no swelling; there were very pronounced milky opacities along the vessels, which were more pronounced on the right; there was considerable exophthalmos. Hearing was normal; the Rinne test was positive. The fifth nerve was normal. There was no remaining facial paralysis. The tongue was rough and fissured; the teeth were in good condition, without pyorrhea; the throat was normal; there was a good palatal reflex. There was no enlargement of the thyroid. The pulse rate was 140, regular in rhythm and soft; the heart was normal. No reflexes were elicited in the arms. There was no pain on pressure over the nerve trunks; the nerves were not palpable; sensation was not impaired to prick and contact. There was pronounced general weakness; movement at the shoulders was fairly good; flexion and extension were moderately strong; there was no wrist-drop; the hand grasp was extremely weak, the left being better than the right. There was pronounced atrophy of the muscles of the forearm and hand, particularly the interossei, and also much median involvement; the "Affenhand" position was present — failure of opposition of the thumbs; there was some tremor, presumably from weakness, but no fibrillation. The thorax was barrel-like. The pectoral muscles were weak. Sensation on the thorax and abdomen was normal to prick and contact. The liver was not enlarged; the abdomen was

slightly tympanitic; the abdominal reflexes were lacking. Both legs were weak, and the patient was unable to stand. There was considerable strength at the hips and knees, and flexion and extension were complete. There was double foot-drop; the toes were strongly flexed on the sole. There was no pain on deep pressure over the nerve trunks; the reflexes were lost; sensation was definitely diminished to prick and touch over the feet and about half way up the legs; sense of position of the great toes was definitely disturbed, perhaps slightly more markedly so on the left than on the right. The feet were rather cold, and the hands were warm.

Four months later, the condition was unchanged, and the patient remained almost totally helpless.

Comment.—The onset was with weakness of the upper extremities, without adequate etiology; there followed paresis of both seventh nerves, ataxic gait, general loss of deep reflexes, weakness of the legs and feet, weakness of the abdominal muscles, and slight persistent disorder of sensation. The spinal fluid showed some increase in cells, entirely out of proportion to the total protein, which at one time reached 708 mg. Partial recovery occurred with, however, continued weakness of the extremities and pronounced atrophy.

In this otherwise typical case, the prognosis for recovery appears to be bad. It is probable that the degenerative process, including the ventral horn cells, has gone so far that recovery is impossible. Apart from slight persistent sensory disturbance and the symmetry of the paralysis, the case at present suggests a poliomyelitis and certainly has certain definite analogies to that disorder.

Case 16.—A boy, aged 7, who was admitted to the Boston Children's Hospital on March 29, 1931, was the second of six living children. Apart from bronchitis during the past winter, with cough and fever of two or three weeks' duration, there was nothing in the history of possible etiologic significance. On March 27, he was slightly irritable and had a poor appetite. On the following day, the legs became so weak that he was unable to walk any distance. On entering the hospital, he complained of a dull aching pain in the posterior part of the thighs, radiating downward. He had been sleeping poorly and had been somewhat nauseated. There had been no exposure to lead.

Physical Examination.—The patient was alert mentally; the pulse rate was 95; the legs were moved with moderate strength, but the movements were apparently limited by pain. He rolled over and sat up with difficulty. The pupils were equal and reacted normally to light and in accommodation. The eyegrounds were normal. The cremasteric and abdominal reflexes were active and equal; the knee jerks were lost. Objectively, sensation was normal. A preliminary diagnosis at the hospital was made of possible poliomyelitis, encephalitis or diffuse neuritis.

On March 30, the spinal fluid was clear, with a pressure of 200, increased globulin, normal sugar, 1 cell, total protein of 100 mg. and sugar, 77 mg.

Course.—On April 2, the hand grasp was weak. On April 7, there was marked general muscular weakness, but no difficulty in swallowing or in respiration. The urine was normal. The hemoglobin measured 90 per cent; the red cells numbered 5,200,000, the white cells, 15,700. On April 14, the spinal fluid was slightly xanthochromic; the pressure was 300, with normal dynamics; the cell count was 1; the total protein, 222 mg. There was at this time a slightly increased hemolysis, indica-

tive of a toxemia or infection. On April 22, there was an elevation of temperature to 101 F., which was unexplained.

On April 23, there was noted a definite internal squint, which was said to be congenital; there was no complaint of diplopia; both external recti muscles were weak, more particularly the right. There was, and had been from the first, definite double facial paresis, the other cranial nerves being free. Lying in bed, the patient was able to raise the arms weakly to a vertical position; the reflexes at the biceps, triceps and wrist were lost; the hand grasps were almost nil; there was no obvious atrophy. The abdominal reflexes were present and active. Some pain was present on deep pressure over the muscles of the thighs and calves, which was more definite in the anterior crural region; there was no further objective or subjective disturbance of sensation. It was entirely impossible for the patient to flex the legs at the hip and to raise them appreciably from the bed. Slight outward rotation of the right leg was possible. All other movements of the legs were practically abolished. The knee and achilles jerks were lost. There was no ankle clonus, and no plantar or Babinski response. There was and had been no sphincter disturbance.

On entrance, 60 cc. of antipoliomyelitic serum was administered intravenously, with no reaction whatever. Except for greater weakness of the legs, the condition had remained essentially unchanged.

The patient died on April 30, of a virulent septic infection (streptococcus) of the throat, after an illness of five days. This infection apparently bore no relation to the original illness. No necropsy was made.

Comment.—Weakness of the legs was followed shortly by double facial paresis, and later by extension of the weakness to the arms, with pain on deep pressure in the legs; there was no mental involvement. The spinal fluid showed a pronounced increase of total protein, with slight xanthochromia and a low cell count.

This case is typical of the symptom complex under consideration in its clinical manifestations and in the spinal fluid observations.

GENERAL COMMENT

Certain facts appear from an analysis of the series of cases reported, the more important of which are as follows:

Little that is definite is to be said regarding a period of latency. An attack of tonsillitis, ordinary colds, so-called influenza and in one instance chickenpox preceded the onset of definite symptoms, but it is difficult to bring any of them or other conditions into a distinct etiologic relationship with the later development of typical symptoms. Much has been said in analogous cases of a preceding infection of the upper respiratory tract (Strauss and Rabiner [23] and Sands [24]), but here again our statistics do not bear out any constant relationship. If an antecedent infection of some sort is to be regarded as significant, the period of latency varies so widely, from a few days to several months, as to be of little diagnostic value. It is our opinion that nothing definite has yet been determined regarding the onset of the disorder in relation to such vague infections.

The statement made by Bradford, Bashford and Wilson [9] regarding the primary involvement of large muscle groups with relative sparing of the distal extremities is in general borne out by our observations. An exception is case 16. As a rule, the legs are first affected, but this is by no means constant. In case 5, for example, the first symptoms were numbness and weakness of the hands, followed by weakness of the legs. In case 14, the first symptoms also appeared in an arm. As a general rule, the facial diplegia appears later, but this also is not constant, as evidenced, for example, by case 3. The not particularly infrequent paralysis of both facial nerves without other symptoms, of which we have observed various examples, may be regarded as an abortive or incomplete form of the symptom complex. Again, it is evident that although other cranial nerves are much less frequently involved than the facial, such disturbances may occur and in fact often do, usually, however, in less complete form. In case 1, for example, there were diplopia and some disorder of sensation in one fifth nerve. In case 7, diplopia was the first symptom, with ptosis on one side and nystagmus. In case 13, there was also diplopia, and in case 14, difficulty in swallowing. It is evident, therefore, that to single out the facial nerves as alone involved is not justified, although this paralysis is in general more pronounced, more constant and clinically more conspicuous than the involvement of other nerves.

The loss of deep reflexes we found practically constant, as in ordinary types of polyneuritis. This does not apply in equal degree to the peripheral reflexes. A certain degree of sensory disorder is constant, and is often described as paresthesias of various sorts combined not infrequently with definite objective signs. Pain on deep pressure over the nerves was frequently observed in our series. The sphincters were somewhat rarely involved and then only for very brief periods. In none of our cases did this continue for more than one or two days.

In no instance in our cases was there any mental disturbance, which indicates that the process does not affect the cortex or, at least, to such a slight degree as to lead to no obvious symptoms. On the whole, it may be said that in the symptom complex under consideration the lesions are limited chiefly to the segments of the spinal cord and the brain stem, in contrast to the possibly allied infections included under the general term of encephalitis. Nothing definite can be said regarding mortality in the somewhat scattered cases hitherto reported. In Bradford's series, under war conditions, eight of thirty patients died, presumably a larger number than under more normal conditions. In our experience, one patient, whose case is not here reported, died, and the patient in case 3 of this series also died after a rapid and stormy course. The prognosis as regards life is, in general, good, although

no exact statistics of value can be given. It is also good as regards symptomatic recovery. In case 1, however, a slight degree of facial paresis has persisted for many years, and in another, not reported, it was practically the only remaining sign after at least fifteen years. In contrast to this, it has been our experience that the facial paralysis is often extremely ephemeral and recovery is absolutely complete.

As a fact, the onset of the disorder, its signs and symptoms and its outcome are so diverse that nothing definite can be said regarding them; a detailed enumeration of their variations is of little value or significance. The only possible generalization is that this infection of the nervous system is characterized mainly by wide-spread muscular weakness, lost deep reflexes and disturbed sensation of the neuritic or neuronitic type, together with a rather selective paresis of the facial nerves. It is impossible to bring the symptomatology into a definitely fixed type.

Etiology.—Until the appearance of the paper by Bradford, Bashford and Wilson in 1918, no definite advance had been made regarding the etiology of this well defined complex of symptoms. On the basis of the observation of thirty cases, twenty of which were carefully reported, these writers came to definite conclusions. Wilson believed that he had isolated and cultivated the virus of the disease, as he was able to make injections into monkeys inoculated with an emulsion of the spinal cord from three human cases and to recover the organism post mortem from the experimental animals. Referring to the work of Flexner and Lewis on poliomyelitis, he believed that he had isolated globoid bodies of similar character which he asserted were the cause of the disease; he concluded that the organisms of poliomyelitis and of so-called infectious polyneuritis have a group relationship, but are nevertheless distinct. So far as is known, this work has not been verified by other investigators. If such a virus is ultimately established, the question will still remain open as to whether or not it or some allied organism is likewise the cause of the various closely related acute infections of which mention has been made. It may perhaps be doubted that the disease produced in monkeys was the same as that appearing in man, especially since no mention is made of facial or other cranial nerve palsies in the animals; it is fair to assume that the mere presence of paralysis of the extremities is not sufficient to establish this relationship.

Pathologic Anatomy.—There is much definite knowledge concerning the pathologic changes, although the descriptions by different writers vary widely, indicating presumably the widespread and diverse character of the lesions produced by the infection. In one of the earliest cases reported by one of us (Dr. Taylor), which evidently belongs to this

group, comparatively few alterations were noted beyond the appearance of numerous amyloid bodies, the significance of which is doubtful, and a definite pigmentary atrophy of nerve cells. No definite alterations were observed in the peripheral nerves or the membranes. Many years apparently passed before further studies were made of patients dying with the symptom complex under consideration. Gordon Holmes,[8] in 1917, studied two cases in which he found myelin degeneration and nothing of consequence in the cortical or cord cells beyond a slight chromatolysis. Bradford found that the histologic changes in Wilson's experimental monkeys were similar to those occurring in man, but were not particularly pronounced. He noted considerable hyperplasia of the lymphatic glands, some congestion at the bases of the papillae of the kidneys and general involvement of the gray matter of the entire nervous system, suggesting a septicemia or systematic poisoning entering the central nervous system by way of the nerve trunks.

In 1919, Casamajor published an admirable description of the pathologic alterations. He found general hyperemia, hemorrhage, swelling of the arachnoid and thickening of the pia, with no changes in the blood vessels. There were an increase of cellular neuroglia in the gray matter, changes in the nerve roots and dorsal root ganglia and slight degeneration of the ventral horns and tract cells, with marked primary and secondary degeneration of the anterior nerve roots on emergence from the pia. There was also degeneration in the dorsal nerve roots outside the dura. For this group of disturbances he suggested the designation meningomyelo-neuronitis, although he did not use this highly descriptive term as the title of his paper. Bassoe [11] pointed out in analogous cases that pial inflammation over the cerebral cortex is relatively marked.

Viets [14] found structural changes in the nuclei of the seventh nerves with chromatolysis and occasional displacement of nuclei. The cells in the anterior horns of the cord, particularly in the cervical and lumbar regions, showed swelling, loss of Nissl granules and displacement of the nuclei, with congestion of the blood vessels. The meninges were normal.

Although differing in detail, it has been definitely established, therefore, that extensive and often profound alterations take place throughout the entire central nervous system as well as in the proximal peripheral nerves, which in general cannot be definitely identified with those occurring in epidemic encephalitis, but yet presumably have a much closer relationship to it than has hitherto been supposed.

Spinal Fluid.—Extensive studies have not been made in the symptom complex of polyneuritis with facial diplegia, nor in the general group of analogous acute infections, with the exception of epidemic ence-

phalitis. In 1916, Guillain [28] described two cases of radiculitis, without facial paralysis, in which he noted a hyperalbuminosis of the spinal fluid without a cytologic reaction (dissociation albumino-cytologique). Bradford found no abnormality in the fluid in four cases. Govaerts [12] was apparently the first to make a careful study of the fluid in a typical case. He reported an "enormous quantity" of albumin, with but 1 lymphocyte. Margulis [18] found no positive serologic or cytologic changes in the spinal fluid.

François and Montus [21] mentioned albumin, cell dissociation and slight xanthochromia in one case. Viets, in 1927, gave a much more detailed description of the spinal fluid. He found a normal initial pressure of 160 mm., rising to 270 mm. on jugular compression; 1 large mononuclear cell; strongly positive alcohol and ammonium sulphate tests; chlorides, 706 mg., sugar, 59 mg., total protein, 348 mg., and nonprotein nitrogen, 348 mg. per hundred cubic centimeters, and a negative Wassermann reaction.

Casamajor reported the fluid as normal. Hendrick, in one case, found the fluid clear, with 2 cells and increased albumin. In one case of myeloradiculitis reported by Strauss and Rabiner, there was a pleocytosis, but otherwise no abnormality of cells or protein content. Sands, on the other hand, found in his series of acute benign infectious myelitis an increase in protein with a slight cellular reaction, as originally described by Guillain and others.

In one of our cases the total protein was 49 mg., somewhat above normal limits; in another, in which the fluid contained 6 cells, it was not increased. Others showed a definite increase to 171 and 222 mg., with a normal cell count (case 16), and to 336 mg., and in one instance (case 15) the total protein reached 708 mg., with a cell count of 169. Particularly noteworthy is case 5, in which the total protein in the cisternal fluid was 49 mg., with 2 lymphocytes, and the spinal fluid 206, with 4 cells. Possibly this disparity between the cisternal and lumbar fluids may indicate a greater involvement of the cord in the pathologic process. Under ordinary conditions of generalized character, such, for example, as multiple sclerosis, no such difference has been observed. A more detailed study of the spinal fluid in this group of cases is desirable; there is already definite evidence that the increased protein content is somewhat characteristic and possibly of diagnostic importance. The colloidal gold curve varies.

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28. Guillain, G.; Barré, J. H., and Strohl, A.: Sur un syndrome de radiculonévrite avec hyperalbuminose du liquide céphalo-rachidien sans réaction cellulaire: Remarques sur les caractères cliniques et graphiques des réflexes tendineux, Bull. et mém. Soc. méd. d. hôp. de Paris **40**:1462, 1916.

In general, it is evident, as might be expected, considering the diversity of the symptomatology, that every part of the central nervous system, including the meninges and the peripheral nerves, particularly in their proximal portions, as well as the spinal fluid, may be involved in a demonstrable pathologic process. Again it is apparent that polyneuritis with facial diplegia represents but one frequently recurring type of response to a general infective agent. We cannot too strongly insist that there is no justification for singling out this symptom complex as independent, except superficially in its striking clinical manifestations.

Clinical Course.—In substantial agreement with others, Bradford reached the following general conclusions regarding the course of the disease: Usually there is a somewhat indefinite history of an initial illness, often with transitory symptoms of fever, headache, pain in the back and vomiting. Of these symptoms, headache is the most constant. After a few days, the patient apparently recovers completely. This so-called period of latency may last for from a few days to five or six weeks, when the more severe or paralytic stage develops. A general muscular weakness comes on rather rapidly and not infrequently suddenly, the patient often falling from weakness. In general, this weakness increases; paresthesias of the extremities appear; headache is common, but fever may not occur, and if so, only to a slight degree. The legs are usually first affected, and, according to Bradford, in no instance were the distal segments of the limbs primarily involved. The arms may later be involved, but always, whether of the arms, legs or body, the paresis is not confined to individual muscles. Involvement of the muscles of the trunk frequently leads to respiratory disturbances. Facial paralysis supervenes as a most characteristic feature of the disorder. Seventeen of the twenty cases studied by Bradford showed facial diplegia. In two no note was made, and in only one was there a definite statement that facial paralysis did not occur. In three cases the paralysis was unilateral. Other cranial nerves are rarely involved; on the sensory side there is a marked and variable disturbance, often largely of the subjective type. The deep reflexes are ultimately lost, whereas the superficial reflexes vary. The pupillary reflexes are not affected; the sphincters may be temporarily involved; the cerebral functions are slightly affected, but no actual mental symptoms ever occur. There may be moderate tachycardia; the blood shows a moderate leukocytosis early in the paralytic stage. The mortality is regarded by Bradford as high, death having occurred in eight of his thirty cases, usually within ten days of the onset of grave symptoms. The patients who survive show, as a rule, a strong tendency toward rapid and complete recovery, none longer in his experience than six months.

A very similar description has been given by Gordon Holmes. In fact, scattered throughout the literature, one finds this symptom complex

in almost identical form appearing so frequently as to have led to the supposition that it represents a distinct disease entity, as, for example, has been somewhat dogmatically stated by Casamajor and Bradford. This idea naturally had further support from the asserted discovery by Bradford, Bashford and Wilson of the causative agent. Although it is now definitely established that a striking combination of signs and symptoms frequently occurs, characterized clinically by double facial paralysis and apparent polyneuritis of widespread distribution, there appears to be little justification for regarding this as a disease *sui generis*. So striking was the occurrence of facial diplegia combined with peripheral nerve symptoms that many writers, beginning with Laurans' comprehensive monograph down to the present time, have been inclined to emphasize what is evidently a frequent but by no means essential part of a widespread series of infections of the nervous system still of unknown etiology, if we except Bradford, Bashford and Wilson's work. Of special interest, therefore, are the closely allied cases that have been described under a wide range of captions. There is much reason to think that the conditions variously termed encephalitis of the epidemic and sporadic types, poliencephalitis, superior and inferior polioencephalomyelitis, encephalitis, Landry's paralysis, poliomyelitis, infectious polyneuritis with facial diplegia, and more recently neuronitis (Kennedy), myeloradiculitis (Strauss and Rabiner) and acute, benign, infectious myelitis (Sands) are due to a common infective agent and therefore should be regarded as varying manifestations of one disease in the sense, for example, that we speak of the diverse symptomatology of syphilis or tuberculosis. It does not conduce to clarity of thinking to speak of diseases until one has a clear picture of the entire morbid process in addition to the obvious clinical course. It is clearly too early, with due regard to Bradford, Bashford and Wilson's unconfirmed work, to assume that a unifying etiologic cause has been discovered. It is therefore more reasonable to consider the increasingly large group of acute infective processes as manifestations of a single or of allied organisms, as yet undemonstrated.

That there is at present no justification for regarding any of these acute infections as individual disease entities is furthermore sufficiently demonstrated by the transitional forms and consequent confused clinical pictures. The tendency to magnify similarities and to minimize differences is well exemplified in this group of disorders in the attempt to establish circumscribed clinical entities. Since the original description by Landry, in 1859, of an ascending paralysis of fatal outcome without pathologic changes sufficient to account for death, a great variety of cases has been published of varied symptomatology under his name, yet there still seems to be a tendency among certain observers to consider so-called Landry's paralysis as a distinct disease. On the whole, how-

ever, the opinion has grown that, except for the ascending type of the paralysis, the symptomatology is so varied that the patronymic has no further justification. In 1895, Walton [14] attempted with considerable success to identify Landry's paralysis with multiple neuritis; in 1900, one of us (Dr. Taylor) discussed the subject of classification, with the conclusion that the term as descriptive of a disease entity should be dropped; Laurans,[2] in 1908, pointed out the similarity between Landry's paralysis and the facial diplegic paralytic form of polyneuritis, and more recently (1925) Stewart [19] has emphasized the same point, although at the same time pointing out what he considers their distinguishing features.

Bériel and Devic [17] thought that certain "Landry-like" cases belong in the polyneuritic group. In general, it may be said that in the light of recent study of the acute infections, especially of the polyneuritic type, the claim of Landry's paralysis as an entity has become still more tenuous and in spite of the unfortunate retention of the name has ceased to exist, and that it should hereafter be considered merely as one of the varieties of development of a general infection. Many of the cases published as Landry's paralysis are evidently transitional forms between a predominantly ascending paralysis, as originally described, and the complicated clinical group of which the polyneuritis under discussion is an outstanding example.

Epidemic encephalitis, originally hailed as a new disease with a supposedly characteristic symptomatology, has gone through a similar evolution since its recent description by von Economo fourteen years ago. As knowledge has grown, this description has been found wholly inadequate to cover its various manifestations. Of present interest is its probable relationship to the symptom complex of polyneuritis and facial paralysis which has been noted by a number of observers. Bassoe,[11] in 1890, reported a series of cases suggesting typhoid fever, miliary tuberculosis, acute chorea and so-called infectious neuronitis, which he regarded as encephalitis since the lesions post mortem were similar to those found in that disease. He noted particularly that pial inflammation over the cerebral cortex was relatively marked and also that facial paralysis occasionally occurred. Speaking of the causative agent, he said: "With some hesitation I suggest that this virus also may produce a syndrome characterized by meningeal irritation and by irritation or paralysis referable to the spinal or cranial nerve roots." Barker, Cross and Irwin,[13] discussing epidemic encephalitis and other infections, were inclined to think that there is an underlying unity with a single infective agent. Sharkne and Moog [16] went somewhat further in their observation of neuritic symptoms developing after encephalitis and expressed the idea that, in addition to ordinary encephalitis, encephalomyelitis, pure myelitis or a neuritis may be due to the same

cause, and finally that a rudimentary form of encephalomyeloneuritis of epidemic character may occur, in which the neuritic element practically alone comes to full development. They concluded that the encephalitic virus at times has a varying affinity for different parts of the nervous system. Bériel and Devic [17] (1925) considered it justifiable to interpret the polyneuritic cases as a manifestation of the virus of encephalitis, enlarging the conception of encephalitis to involve the cord and peripheral nerves and even the neuromuscular apparatus. They considered the meninges as a possible point of invasion of the virus and suggested the term peripheral encephalitis. Margulis (1926) reported a case in which polyneuritis developed in connection with unquestioned epidemic encephalitis. Sands (1931), under the title "Acute Benign Infectious Myelitis," described an important group of cases, somewhat similar to those of Strauss and Rabiner, and suggested their possible relationship to epidemic encephalitis.

Such references might be multiplied, but those given are sufficient to emphasize the point that many writers have been impressed with the fact that these infections described under diverse names may be variations of epidemic encephalitis, or, more correctly stated, are due to a common virus of which encephalitis is one of the outstanding manifestations.

It is, furthermore, evident that before encephalitis in its epidemic form was generally known, following von Economo's description in 1917, cases had been reported of Landry's paralysis, poliencephalitis and polioencephalomyelitis which correspond precisely to polyneuritis with facial diplegia, such, for example, as those reported by one of us (Dr. Taylor), to which allusion has already been made. The further one looks the more obvious it becomes that for many years a great variety of clinical syndromes has been described which have been dignified as disease entities, but which on more careful study show so many transitional forms that such a demarcation is by no means justified. What future investigation may demonstrate is purely a matter of speculation, but until a definite etiologic factor or factors are determined, the best working hypothesis is to get away from the "entity" idea and consider the whole group of infections as varying manifestations of a common cause.

CONCLUSIONS

Sixteen cases are reported, fourteen of polyneuritis with facial diplegia, one of polyneuritis without definite facial paresis and one of double facial involvement and paresis of other cranial nerves without involvement of the extremities.

From a study of these and other cases reported, it is evident that the syndrome is of relatively frequent occurrence, that it is sporadic and never appears in epidemic form, and that it is not confined to adult life.

The etiology has not been definitely determined. The signs of infection are slight and often entirely absent. A febrile onset is inconstant. No fixed latency period, therefore, can be determined.

The symptomatology, apart from the somewhat arbitrary coincidence of facial diplegia and general peripheral neuritis or neuronitis, is varied.

No constant relationship exists between the appearance of the facial paresis and the more general signs of neuritis.

The duration of the disease is from one or two weeks to several months.

Death, from respiratory involvement, is rare. Complete recovery is the usual outcome. Occasionally, full facial control does not return.

Pathologic changes are of the nature of a diffuse inflammation, involving especially peripheral neurons, the cord and brain stem to a lesser extent and the cortex slightly if at all.

The cerebrospinal fluid varies from normal to a condition characterized by a pronounced increase in total protein with slight or often no increase in the number of cells (albuminocellular dissociation—Guillain).

Further detailed study of the serology of the cerebrospinal fluid from the lumbar, cisternal and ventricular regions should yield results of importance from a diagnostic standpoint.

NEUROSOMATIC DETERIORATION IN EPILEPSY

A CLINICOPATHOLOGIC CONTRIBUTION TO THE CONCEPT WITH A REPORT OF TWO CASES *

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In a previous paper [1] we expressed the view that the progressive changes developing in persons with epilepsy in the course of time have a definite symptomatology and evolution which can be described in neurologic terms. We called these progressive neurologic changes "neurosomatic deterioration." Derived solely from clinical observations, this view was a purely clinical concept; it was natural, therefore, that we looked for an opportunity to study the pathologic changes that might underlie the symptomatology of deterioration.

Two cases have come to autopsy, and as both of them had fairly complete case histories these brains were submitted to microscopic study.

REPORT OF CASES

CASE 1.—*History.*—Irven G., a boy, aged 12, was admitted to the Monson State Hospital because of epilepsy and advanced mental and physical deterioration. The family history was negative as to epilepsy, nervous or mental disease, alcoholism and syphilis. Both parents are living and in good health. The mother had had nine pregnancies; the first children—twins—both died in early infancy, one of congenital heart trouble, the other of some acute gastro-intestinal disorder; the second resulted in an abortion at six months; then she had seven living children of whom the second died at 9 months of "spinal meningitis"; the sixth is the patient. The other five children are in good health and of normal mental and physical development.

The patient was born at full term by normal labor. He had no illnesses except whooping cough at 8 months and measles at 18 months. He had no convulsions, spasms or other complications accompanying or following these illnesses. He cut his first tooth at 5 months, and teething was not difficult. He began to talk at 1 year of age and walked at 13 months. He was a strong and healthy baby until 1918, when at 3½ years of age he had influenza; he was ill for several weeks, had a high fever and was delirious. A week after he was taken ill, the mother noticed

* Submitted for publication, May 15, 1931.

* From the Monson State Hospital.

* Prof. Stanley Cobb of the Harvard Medical School permitted us to use the resources of his laboratory, and aided us especially by his advice and guidance during the study of microscopic sections.

1. Hodskins, M. B., and Yakovlev, P. I.: Neurosomatic Deterioration in Epilepsy, Arch. Neurol. & Psychiat. **23**:986 (May) 1930.

that the left arm and leg were paralyzed. He recovered from this illness and the paralysis cleared up, but a month later he had a first epileptic attack. As he grew older the attacks became more severe. When 6 years of age, he was admitted to a state school for feebleminded children where he remained for six years. An abstract of the records of this institution states: "Talks little except to swear; will sit about with dropped head—a typical picture of the terminal stage of epilepsy. The epileptic convulsions are fairly frequent, although lately he goes almost a month with only one or two. At other times he will have seventeen or more in a series." On Aug. 12, 1927, he was admitted to the Monson State Hospital.

Physical Examination.—The boy was poorly nourished and developed. The shape of the head was normal; the face was symmetrical. There were no stigmas of degeneration. The extremities were cold, clammy and cyanotic. The heart sounds were of fair quality; no murmurs were heard. The lungs were normal. The liver and spleen were not palpable; the abdomen was normal. Urinalysis gave negative results. A Wassermann test of the blood was negative.

Neurologic Examination.—After admission, the patient was permanently confined to bed and did not show any spontaneous impulse to walk. His habitual body position was characteristic: the lower extremities were flexed at the knees and hips, the thighs drawn up on the abdomen; spontaneous voluntary movements in the lower extremities were reduced to a minimum; however, when uncovered, one observed sometimes that the patient could extend the flexed lower extremities in a slow and incomplete fashion; the thighs were always in adduction, the knees tightly pressed together; the feet were plantar flexed and outwardly rotated, the toes pointing down; there were no tendinous retractions in the knee joints, but a moderate shortening of the achilles tendon on both sides prevented a full dorsal flexion of the ankle; some retractures were present in the flexors of the toes; in the upper extremities a considerable amount of spontaneous voluntary movement was present; the usual position of the upper extremities was cross-flexion on the chest, so that the fists were under the chin; however, when disturbed, the patient spontaneously changed this position, bringing the hands onto the flexed knee, or putting one or both hands under the head.

When forced out of bed the patient could stand on his feet and was able to take a few steps. The attitude of the body was typical: it was rigid and stiff in all segments, the head bent on the chest, the trunk inclined forward, the shoulders and thighs adducted, with flexion at the elbow, hip and knees, the arms held stiffly, the hands in a semiclosed position, while the knees were tightly adducted and the feet were spread apart and everted. The stonelike immobility of the body appeared to be distinctly increased when the patient was forced to stand on his feet. The face, especially the lower part, appeared masklike and inexpressive, as if frozen. The lower jaw drooped, and strings of saliva drooled from the corners of the mouth. The patient had a vacant look. If pushed, he took a few short, irregular steps, and if one insisted in making him walk, he stumbled and eventually would fall, as in one piece. The gait was spastic. The muscular hypertonia increased with the effort to keep erect and walk. When the arms were extended and the fingers spread, there was a tremor in both hands. Passive movements of the extremities revealed a distinct antagonistic resistance with irregular intermittent or remittent rigidity. This muscular rigidity, though generalized throughout the body, distinctly predominated in the proximal parts of the extremities and was more pronounced in the lower than in the upper extremities. In the lower extremities the contracture of the flexors was especially intense, the antagonistic

resistance on passive extension of the leg being distinctly greater than on passive flexion. The same feature was present in the upper extremities, but in a much less degree. The patellar reflexes were exaggerated and hypertonic, with a pronounced hamstring phenomenon and fixation of the leg in the extension phase. The radial and ulnar reflexes were exaggerated and hypertonic. The plantar reflex on the left side was of extensor type; on the right side the response was dull and showed a tendency to extension. The pupils were equal; both reacted to light very sluggishly. Mastication was slow; swallowing was difficult; the patient choked, and liquids were regurgitated through the nose. He did not talk spontaneously and swore when disturbed. He was untidy, but not incontinent; there was no retention, no automatic micturition and no dribbling. The patient had no bed sores or other lesions of a neurotrophic type.

Convulsions.—During August, after admission there was recorded only one severe epileptic attack; in September, a series of twelve; in October, six; in November he had a series of thirty-nine severe subintrant epileptic convulsions which resulted in death on November 16, at 12 years 8 months of age, nine years after the onset of the first symptom of epilepsy.

Comment.—The symptomatology and the evolution of the condition in this case were typical of the series of cases we have described in the previous publication.[1] Except for a miscarriage and a pair of twins who died in infancy, the other children of the same stock were in good health and apparently of average mental development. Up to the age of 3½ years the patient was in good health and developed normally. At 3½ years of age he had an acute illness, probably influenzal encephalitis, which caused the primary cerebral lesion. The latter was evident from the fact that the acute illness was complicated with a left-sided paralysis and followed by epileptic convulsions. From that time on deterioration set in and followed a definite course. Two and a half years later, the mental condition necessitated admission to a school for the feebleminded. While in this institution he developed a characteristic akineto-hypertonic syndrome as is evident by the abstract of the medical record. This record testifies also to another feature pertaining to the course of convulsions and to which we drew attention in our earlier publication: the convulsions on the whole diminished in frequency: "lately he goes almost a month with only one or two" but at the same time, instead of frequent isolated seizures, the patient showed a tendency to fits in series. "At times he will have seventeen or nineteen in a series." The deterioration followed a slow but steady progress, and when he came under our observation at the age of 12 years he presented a full blown picture of an advanced stage of neurosomatic deterioration—generalized muscular rigidity, flexion attitude of the head, trunk and extremities, contracture of flexors predominating in the lower extremities, bilateral extensor response, symptoms of pseudobulbar type and profound dementia.

Pathologic Examination.—Autopsy was performed six hours after death. The body was greatly emaciated. Postmortem rigidity fixed the attitude that had been characteristic during the latter part of life: flexion of the lower extremities on the abdomen and flexion of the upper extremities on the chest, with the fists closed and brought under the chin.

Thoracic Cavity: The thymus gland was in a state of full involution; only slight rudiments were found. The pleural cavity contained about 50 cc. of fluid. Pleural adhesions were present over the posterior aspect of the apex of the right lung. The lymph glands of the hilus were not enlarged. The lungs were of pale grayish color, without indurations, crepitated on pressure, and yielded on section a white foamy fluid. The heart was small (115 Gm.); the left ventricle contained a well formed blood clot extending into the aorta; about 20 cc. of fluid was present in the pericardial sac. The heart muscle, orifices and valves appeared to be normal.

Abdominal Cavity: The transverse and descending colon was much distended. The hepatic and splenic flexures were about three times smaller in diameter than the rest of the colon, without evidence of scars or peritoneal adhesions. The liver was small and hard (475 Gm.); the surface was finely granular, with whitish-yellow, irregular, patchy areas; the capsule was adherent, especially beneath these areas; it was pale and the section was granular and grayish, with yellow streaks; on palpation, minute nodulations were felt. The spleen appeared normal (35 Gm.). The left (52 Gm.) and right kidneys (60 Gm.) were found to be normal; the capsules were not adherent. The left (1.4 Gm.) and right (1 Gm.) suprarenal glands showed on the cut surface a few minute hemorrhagic spots. The pancreas (50 Gm.) was normal. The remaining abdominal organs, on gross inspection, did not present anything unusual.

Head and Cranial Cavity: The calvarium was easily detached from the dura, which was normal. After incision, a clear cerebrospinal fluid escaped. The dura was adherent to the hemispheres along the longitudinal fissures. Pacchionian bodies were well developed and were calcified. A few adhesions were found on the convex surface of the brain over the parietal, occipital and temporal lobes. The cerebral hemispheres were of normal size but much harder in consistency than usual. The gyri were flattened, as if under pressure. The pia had a normal appearance. The pial vessels were congested. The external configurations of the brain and cerebellum did not show anything abnormal. Section of the cerebral hemisphere showed considerable dilatation of the lateral ventricles. The cortex appeared to be somewhat thin. The weight of the brain and cerebellum was 1,200 Gm.

The spinal cord was removed, and macroscopic examination did not show anything abnormal.

Histopathologic Studies.—Small pieces of liver, spleen and pancreas were put into Zenker's solution. The brain and spinal cord were placed in diluted solution of formaldehyde, U. S. P. (1:10).

Liver: Stained with hematoxylin and eosin, the liver showed a diffuse increase of connective tissue but no bands or special distribution of it. The blood spaces were congested. There were a few pinpoint hemorrhages and acute degeneration of liver cells with vacuolization and agonal and postmortem alterations. The capsule was thickened.

Spleen: Stained with hematoxylin and eosin, the spleen showed congestion and thickening of the vessel walls, especially of the arteries; otherwise the organ was normal.

Pancreas: Stained with hematoxylin and eosin, the pancreas showed congestion. There was an acute degeneration, with vacuoles in the cells, and agonal and postmortem alterations.

Brain: The tissue was well hardened, and small pieces from different convolutions of the frontal, parietal and occipital cortex, larger pieces from the basal ganglia and pedunculo-hypothalamic region, from the cerebellar cortex and dentate nucleus, from the pons, medulla and the three levels of the spinal cord were taken for sections. Most of the microscopic preparations were made with frozen sections. A fairly complete series of Nissl, van Gieson and Spielmeyer stains were made from pieces of each region; a few stained with hematoxylin-eosin, scarlet red and the Weigert method (from the medulla and spinal cord) were added.

The cerebral cortex in general showed marked capillary and venous congestion, with some hemorrhage into the subarachnoid space and a few perivascular extravasations. In several places there were large empty veins and in others collections of cavernous veins. The pia was thick and infiltrated with lymphocytes, plasma cells and gitter cells. A few rod cells were found free; in one place (parietal region) there was a small hemorrhage that was partly organized. The walls of the arteries were thicker than one would expect in a child. The perivascular spaces were wide. A few empty spaces, like veins, were seen lined with endothelium but containing no blood. In other places small groups of large veins were found together, making almost a cavernous tissue. Following the periphery of the cortical section, one found thickened pia-arachnoid adherent to the cortex, and underneath these adhesions a fibrous overgrowth of marginal glia penetrating into and interlacing with the pial fiber cells. The overgrowth of a thick meshwork of glia fibers under the pia on the periphery of the cortex could be followed throughout several sections and appeared to be especially pronounced in the frontal region. There was a considerable degree of marginal gliosis.

All six laminae of the cortex could be differentiated in all sections; however, in sections from the frontal cortex and to a lesser extent in sections from the occipital cortex, in some places this differentiation became difficult as the most characteristic landmarks of the third and fifth layers were considerably changed as to the number and morphology of their cellular elements.

Frontal Cortex: Left hemisphere: On the whole, the sections from the frontal cortex showed the most conspicuous pathologic changes, especially in the third and to some extent in the fifth lamina. The number of large pyramidal cells appeared to be reduced. Many nerve cells were shrunken, and showed vacuoles in the cytoplasm and eccentric nuclei. Many cells in the fifth lamina, epecially, had eccentric nuclei and darkly stained homogeneous protoplasm. With the scarlet red stain, fat was found in almost every pyramidal cell (fig. 1). The third and fifth laminae were more conspicuously affected than the outer laminae. The small blood vessels were congested, and there was an occasional blood extravasation.

Parietal Cortex: Left hemisphere: Numerous ganglion cells in this region appeared to be in a good condition. Many others showed distinct cytomorphologic changes. Many of the cells were shrunken. Occasionally, large swollen cells with pale cloudy cell bodies, eccentric, poorly outlined nuclei and thick, distorted dendrites were found. The Nissl substance in these cells was reduced, appearing dustlike. Gitter cells and neuronophagic pictures were frequently encountered. The third layer was especially the seat of these cell changes.

Occipital Cortex: The picture of cytomorphologic changes was more severe than in the parietal cortex. There were many shrunken cells with hyperchromatic homogeneous protoplasm and eccentric nuclei, with rich intracellular fat deposits.

Diencephalon and Pedunculo-Hypothalamic Formations: The basal ganglia were more affected than the cortex, especially with regard to the more advanced vascular changes and also with regard to the secondary gliosis that replaced the devastated nerve cells, the changes in which were similar to those in the cortex. They appeared to be, however, more conspicuous and more varied. Studying the sections from the different gray formations of the subcortical region, one found that sections from the pallidum and pedunculo-hypothalamic region (corpus luysii and

Fig. 1 (case 1).—Frontal cortex, showing fat-laden ganglion cells of the third layer; scarlet red.

red nucleus) exhibited far more profound lesions than those from the thalamus, caudate nucleus and putamen (fig. 2).

Globus Pallidus: The vascularity of this nucleus was tremendously increased. The vessel walls were thickened, often calcified, the tunica intima split off from the media; the small arterioles had a corkscrew appearance, and the enormously proliferated capillaries were sharply angulated. The veins were often drawn into groups and knots. Throughout this section one found small pinholes of mucoid degeneration. A profuse overgrowth of glia fibers and numerous glia nuclei were

another striking characteristic of this formation. The typical large pallidal nerve cells were greatly diminished in number and distributed with extreme irregularity into islands of from five to twenty cells, separated by the clear zones of cell devastation filled with glia. The remaining ganglion cells showed chronic and acute changes: swelling of cell bodies with heavy dendrites, chronic shrinkage with dark hyperstained and homogeneous protoplasm. Many nerve cells were found in a state of cytolysis, with an irregularly outlined cell body containing sometimes large vacuoles and an indistinct nucleus. The nuclei were often split, and some of them

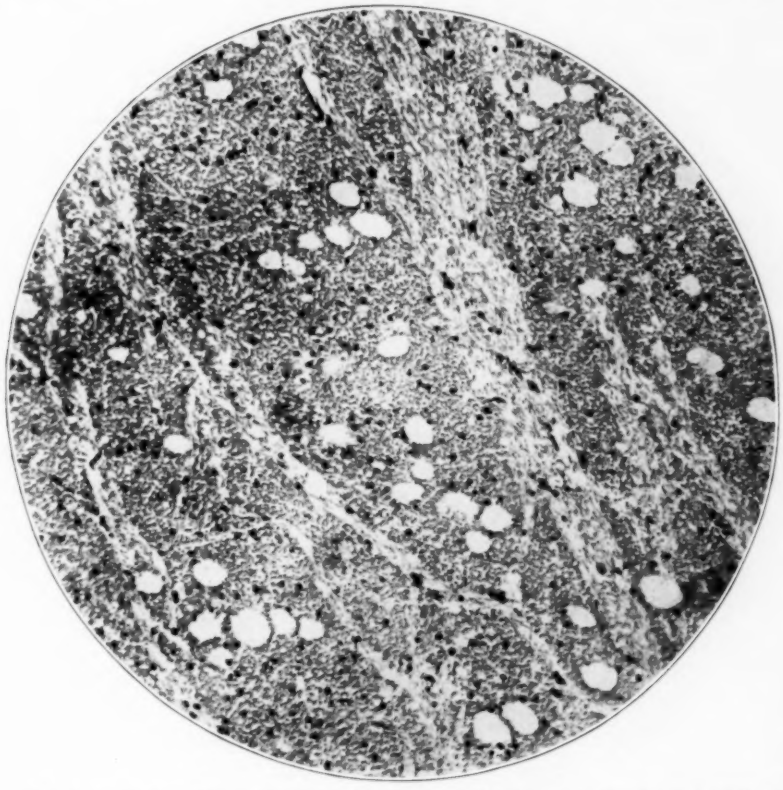

Fig. 2 (case 1).—Hypothalamus, showing mucoid degeneration; hematoxylin and eosin.

were also vacuolated. All degrees of neuronophagia were observed, from simple exaggerated satellitosis to the formation of glial clusters around fragments of a disintegrated cell; of the small pallidal cells only a few remained, and these showed degenerative alteration (fig. 3).

Putamen and Caudate Nucleus: Both nuclei showed proliferation of capillaries, fibroglial overgrowth and many cytomorphologic changes—eccentric nuclei, acute swelling, shrinking, breaking up of Nissl substance, dark homogeneous cytoplasm and neuronophagia

Thalamus: This body showed similar changes, though they were not so pronounced. The number of cells in the pulvinar appeared to be somewhat diminished.

There were numerous glia nuclei. Many cells were shrunken. Most of the cells had eccentric nuclei.

Corpus Luysii and Red Nucleus: These structures were the seat of conspicuous changes, especially the first, which in this respect was comparable to the globus pallidus, without, however, so much of the secondary sclerotic alterations. In the red nucleus axonal reactions were especially conspicuous, but many cells were severely shrunken and showed satellitosis (fig. 4).

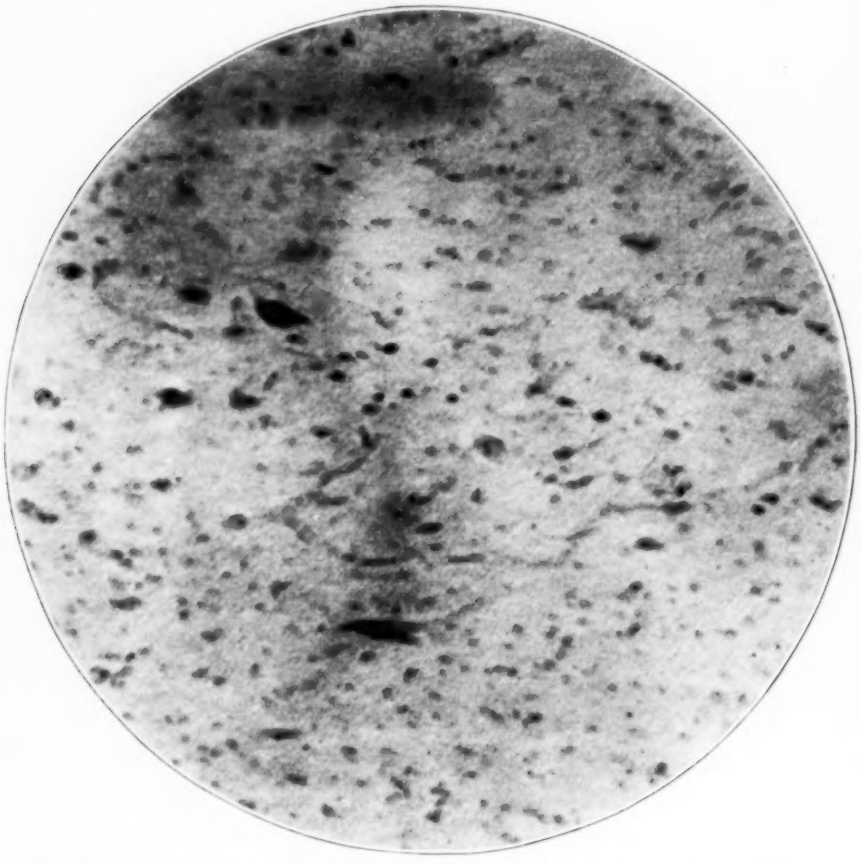

Fig. 3 (case 1).—Pallidum. Note the karyorrhexis, elongated shrunken bodies; some are swollen, rounded up; proliferation of glia nuclei (progressive gliosis); Nissl methylene blue (methylthionine chloride U. S. P.).

Unfortunately, in cutting sections from the peduncular region, the substantia nigra was missed.

The wall of the third ventricle showed irregularly festooned ependyma and a dense subependymal overgrowth or glia without nuclei.

Cerebellum and Dentate Nucleus: The cerebellum was involved by the same diffuse degenerative process as the cortex and basal ganglia, though to a lesser degree. All three laminae of the cerebellar cortex were well developed; however,

the string of Purkinje cells showed occasional gaps where the cells had dropped out; those that remained were often pale with an obscure nuclear outline, and sometimes the nucleolus was missing. Many cells were present in a relatively good condition. In the dentate nucleus the nerve cells were somewhat fewer than normal, and the fat stain showed that many were filled with pin-sized fat granules. Occasional places were seen where the cells were lacking and glia nuclei and fibrils replaced them. Many cells were pale and swollen, and had eccentric nuclei.

Pons: No sections from this region were available.

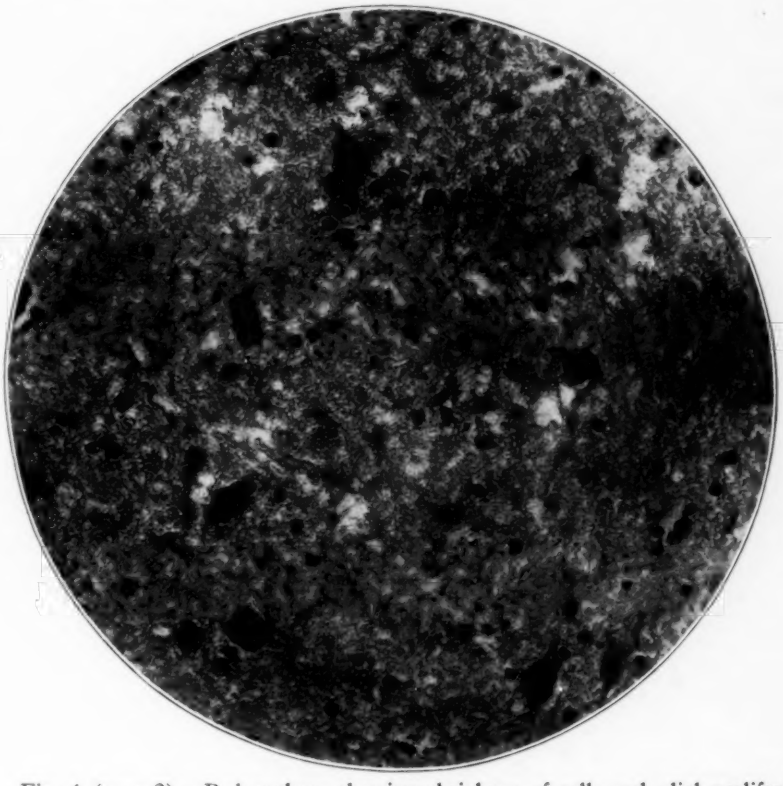

Fig. 4 (case 2).—Red nucleus, showing shrinkage of cells and glial proliferation; hematoxylin and eosin.

Medulla: There was marked congestion of all the blood vessels, especially the small veins; here and there was an extravasion of blood into the perivascular spaces. There was no inflammatory infiltration with leukocytes. The ganglion cells showed acute ischemic swelling and shrinkage. The main picture was one of extreme congestion. This was probably agonal, associated with death in convulsions.

Spinal Cord: Sections from the cervical, dorsal and lumbar regions were normal with the exception of a moderate congestion of the blood vessels. The anterior horn cells were well preserved.

Comment.—It appears from the microscopic study of the lesions in the central nervous system that there is a diffuse pathologic process,

which spares the spinal cord and massively involves the cerebrum. Three main types of lesions can be discriminated in the latter: (1) old, largely organized, inflammatory vascular lesions affecting especially the basal ganglia and the cortex; (2) a chronic evolutive process of atrophic and degenerative nature, secondary to the primary vascular inflammatory cerebral lesion; these secondary changes were most prominent in the third and fifth laminae of the frontal cortex, in the pallidum and pedunculo-hypothalamic formations; (3) acute congestive and anoxemic lesions confined almost exclusively to the medulla.

Evidence of an old inflammatory lesion is shown by the vascular changes, especially those in the basal ganglia and in the cortex. These vascular changes consist of an intense proliferation and thickening of the walls of capillaries, veins and arteries, calcification of vessel walls and thickening of the pia with many adhesions to the cortex (chronic leptomeningitis). The formation of an almost cavernous tissue in the places where the veins were agglomerated into groups and knots is of interest in connection with the observations of Cobb [2] on vascular lesions in chronic encephalitis. We have good evidence of an old organized meningo-encephalitis, which was particularly severe in the basal ganglia. The acute illness that this patient had in 1918, when 3½ years of age, with delirium, fever, symptoms of meningitis and pneumonia, and partial paralysis, was probably the cause of this inflammatory cerebral lesion.

The primary cerebral lesion was followed by an apparent improvement. The partial left paralysis cleared up; however, grave and progressive symptoms set in soon afterward, testifying that the acute vascular lesion was followed by a chronic evolutive process that kept on, gradually becoming more diffuse. This chronic secondary process consisted of: (*a*) dropping out of nerve cells; (*b*) diffuse secondary gliosis with proliferation of fibroglia and of glia nuclei, marginal gliosis and subependymal gliosis; (*c*) chronic atrophy and degeneration of nerve cells, shrinking, cytolytic changes, mucoid degeneration and fatty degeneration.

Though eminently diffuse, the secondary lesions were distinctly more pronounced in the cortex and in the basal ganglia than elsewhere in the brain. In the cortex, the frontal lobes were most affected. The basal ganglia, globus pallidus, corpus luysii and red nucleus were injured with greater severity than the other nuclei. We believe that this chronic secondary degenerative process, especially the secondary gliosis and atrophic nerve cell changes, can be regarded as the pathology of neurosomatic deterioration. The prominence of the lesions in the large

2. Cobb, S.: Vascular Lesions in a Case of Chronic Encephalitis Lethargica, with Parkinson Syndrome, Arch. Neurol. & Psychiat. **16**:240 (Aug.) 1926.

cells of the third and fifth laminae of the frontal cortex and in the globus pallidus seems to be of particular interest in relation to the fundamental features of the clinical symptomatology in the case, that is, the progressive dementia and the akineto-hypertonic symptom complex (progressive rigidity).

Going further into the correlation between the clinical course of the case and the postmortem pathologic observations, one sees that the patient died following a long series of convulsions which ended in status. The acute and severe circulatory changes in the brain associated with convulsions are a constant phenomenon. Spielmeyer [3] pointed out the acute ischemic cell changes in the brains of persons with epilepsy resulting from such circulatory disturbances. Gildea and Cobb [4] experimentally produced similar ischemic changes in the brains of animals. In our case there is a sufficiently evident and adequate counterpart of such acute circulatory disturbances associated with acute ischemic lesions of the nerve parenchyma, affecting particularly the medulla. It is these medullary changes, constant in patients who have died in epileptic attacks or in status epilepticus, that led Schroeder van der Kolk [5] and later Nothnagel to build up the so-called bulbar theory of convulsions. These changes in the medulla oblongata are terminal and may explain the death by acute bulbar paralysis that results from status epilepticus. The changes in the viscera in our case—heart arrested in diastole, distended intestines, lungs filled with serous fluid and mucus—seem to justify this deduction.

CASE 2.—*History.*—Thomas D., who was born on Aug. 18, 1862, and died in coma following chronic nephritis and arteriosclerosis on March 7, 1928, was of English origin. One brother had died suddenly ("dropped dead") at 57. Another brother died of epidemic influenza at about the same age. Three other brothers are living and well. The patient attended school and went to the fourth standard. He went to work at 8 years of age on half time; at 13 he worked full time, mostly in cotton mills; later he worked as a machinist. In 1911, when 49 years of age, he came to the United States and continued to work as a machinist in cotton mills. Two years later, in 1913, when 51 years of age, he had a first epileptic attack; he has had them ever since. They were at first only of petit mal type; he would lose consciousness, talk incoherently and appear confused for a while, but he had no convulsions. Later, the attacks became more severe; he would fall, have convulsions and bite his cheek; consciousness was always lost. In the course of time, the general condition gradually failed; he became irritable, depressed and forgetful. On July 2, 1927, of his own volition, he was admitted to the Monson State Hospital.

3. Spielmeyer, W.: The Anatomic Substratum of the Convulsive State, Arch. Neurol. & Psychiat. **23**:869 (May) 1930.

4. Gildea, E. F., and Cobb, S.: The Effects of Anemia on the Cerebral Cortex of the Cat, Arch. Neurol. & Psychiat. **23**:876 (May) 1930.

5. van der Kolk, Schroeder, quoted by Féré, C.: Les épilepsies et les épileptiques, Paris, F. Alcan, 1890.

On admission, he complained of epileptic attacks, shortness of breath, insomnia, general weakness and loss of weight. From the social information it was learned later that he used to drink to a considerable extent.

Physical Examination.—The patient was well developed but rather emaciated, looking older than his age. The lungs were normal. The left side of the chest over the heart was more prominent than the right. The heart was enlarged, and presented a "bruit de galop." The blood pressure was 178 systolic and 98 diastolic. The Wassermann reaction of the blood was negative. The urine was diminished in quantity and contained albumin. Mentally, the patient was fairly well oriented, somewhat depressed and at times talkative and childish.

Neurologic Examination (Aug. 9, 1927).—The attitude of the body was somewhat stooped. There was a distinct tremor of both hands. There were deformities of the last two phalanges of the third, fourth and fifth fingers on both hands; the heads of these phalanges were enlarged, and full extension of the fingers was impossible. The patient said that he had had this deformity of the fingers as long as he could remember; the joints looked as if the onset had been in later life, though it was evidently of long duration.

Muscle tonus was increased in the neck, trunk and extremities. A distinct cog-wheel phenomenon was present on passive flexion and extension of the elbows on both sides. Cog-wheel resistance was observed also on passive extension and flexion of both knee joints. The reaction of antagonists was greatly exaggerated. The tonic postural reflexes were exaggerated, especially in the right ankle. The gait on the whole was not impaired, except for some rigidity in the head and trunk and a distinct lack of associated movements, particularly in the right arm. The tendinous reflexes of the upper and lower extremities were all present and typically hypertonic—reduced in amplitude, intense, but of relatively high threshold—and they were not diffuse. The patellar reflexes on both sides were particularly characteristic, with highly exaggerated antagonistic contraction of the hamstrings. The plantar reflex was flexor on both sides. The cremasteric reflex was present on both sides. The abdominal reflexes were not obtained. The abdominal muscles were rigid and tense. There were no combined flexion sign and no foot clonus. Reflexes of defense: the emotional reaction to unpleasant stimuli appeared to be much reduced; on pinching the skin of the ankle no emotional or motor reaction ensued. No sensory disturbances were present. Hearing was somewhat impaired. Vision was diminished on account of presbyopia. The face was symmetrical. The eye movements were free; there was no nystagmus. The pupil reflexes were normal. There was no paralysis of the cranial nerves. Speech was not impaired. The facial expression was somewhat immobile and masklike. So long as the patient was engaged in a conversation, the activity of the facial muscles did not show anything abnormal, but if he was left alone a slight drooping of the lower jaw took place and the lower part of the face had a "frozen" appearance.

Course.—From the time of admission on July 2, 1927, to January, 1928, the patient had a few attacks of petit mal, usually announced by a sensation of vertigo and followed by ambulatory automatism and complete amnesia. During this period he had one severe epileptic attack. Urinalysis constantly showed the presence of albumin, with epithelial and fatty casts. The amount of urine was much diminished (from 750 to 600 cc. per twenty-four hours). The blood pressure remained high. Reduplication of the first heart beat was always present. The general condition of the patient steadily failed.

Reexamination (Jan. 31, 1928).—There were: tremor of the fingers; cog-wheel phenomenon on both sides; hypertonic tendinous reflexes; flexor plantar reflexes;

combined flexion sign with an Oppenheim sign on the right. On testing for reflexes of defense, an overactive hyperalgesic emotional reaction was observed. Fibrillary and fascicular muscular contractions were present in the pectorals and the muscles of the arms, thighs and back. The patient was often disoriented, excessively talkative and sometimes incoherent. The blood pressure was 200 systolic and 50 diastolic. A "bruit de galop" was present. Albumin was present in the urine in large amount.

Subsequent Course.—During February, symptoms of uremia developed. The patient was confined to bed and was much distressed by shortness of breath. The blood pressure remained high. There appeared some edema of the legs and morning puffiness of the face. The quantity of urine fell to 250 cc. per twenty-four hours. After March 4, the patient was in a state of coma, and he died on March 7, 1928, aged 65½ years.

Comment.—It is obvious that in case 2 there was cerebral arteriosclerosis in an aged man with chronic nephritis, high blood pressure and cardiovascular disturbances. The epileptic attacks, which in this case developed after the age of 51, have a different clinical meaning from those in the first case, a child, aged 12, with postencephalitic epilepsy. The basis of the progressive deteriorative changes in case 2 was cerebral arteriosclerosis with chronic nephritis. The patient died in coma. The neurosomatic deterioration in this case was an arteriosclerotic deterioration, showing parkinsonian symptoms as described by Critchley.[6] In our previous publication,[1] we pointed out the clinical analogy of both the symptomatology and the evolution of neourosomatic deterioration in epilepsy and in arteriosclerotic parkinsonism. Indeed, this case has all the requisites necessary for an illustration of neurosomatic deterioration. There is epilepsy, a progressive akineto-hypertonic symptom complex, with typical postural changes, generalized rigidity and tremor; there is an association of pyramidal symptoms in the terminal period (combined flexion, Oppenheim sign). There is a coincident shift of emotional reaction to painful stimuli from emotional indifference to emotional hyperalgesia. There is progressive dementia.

Postmortem Examination.—Autopsy was performed on March 8, 1928, twenty-four hours after death.

Thoracic Cavity: The pleural cavity contained a large amount of transparent yellowish fluid. A few old adhesions were present over the posterior aspect of the left lung. Both lungs, especially the left, were much congested and edematous. The left lung weighed 1,100 Gm.; the right, 750 Gm. The heart was much enlarged, to about twice its normal size; the left ventricle was hypertrophied; the heart muscle on section appeared of brownish color and very soft; the mitral valves showed considerable stenosis, with calcareous deposits in the valves. The aorta appeared normal. The right ventricle contained a blood clot with a yellow fibrinous coagulum. The heart weighed 565 Gm.

Abdominal Cavity: The peritoneal cavity contained much clear ascitic fluid. The liver (1,375 Gm.) was small, gray and of hard consistency; the capsule was

6. Critchley, Macdonald: Arteriosclerotic Parkinsonism, Brain **52**:23, 1929.

adherent; on section the liver substance was gray, finely nodulated and sclerotic in appearance. The gastro-intestinal tract did not show anything unusual. The spleen was small and bluish red. The left kidney (100 Gm.) was small and contained a cyst, the size of a walnut, over the outer and posterior aspect; the capsule stripped off easily; on section, the cortical and medullary substances were not differentiated. The right kidney (90 Gm.) was small; the cortical and the medullary matter were not differentiated; the capsule stripped off easily.

Cranial Cavity: The calvarium was easily detached from the dura. The dura was thick, not transparent, and of whitish color. After incision a large amount of spinal fluid escaped. The dura was adherent to the brain cortex along the longitudinal sinus. The pia was transparent and edematous. The cerebral hemispheres were very hard, and the frontal lobes appeared atrophied, with shrunken convolutions and deepened sulci. The basilar arteries showed pronounced arteriosclerosis. The weight of the brain and cerebellum was 1,490 Gm. The spinal cord was not removed.

Histopathologic Examination.—The study was conducted in the same manner and with the same histologic technic on frozen sections as in case 1. Series of Nissl, van Gieson and Spielmeyer stains, a few hematoxylin and eosin stains and a few Weigert preparations from the medulla oblongata, cervical cord and dentate nucleus were made from celloidin blocks.

Meninges: The membranes were very edematuus; the subarachnoidal spaces are distended, and along the trabeculae and around the vessel walls one found many light-refracting, dark stained, pigmented corpuscles. The meningeal vessels appeared to be increased in number; often they occurred in groups and had thickened walls.

Cerebral Cortex: Vascularization of the cortex and of the subcortical white matter was much increased, mostly by the venous elements and by proliferated capillaries. The perivascular and perineural spaces were much dilated (from edema?), and were free of any round cell infiltration. From the cortical periphery toward the white substance, shot off long pial invaginations, carrying vessels and containing corkscrew-shaped arteries with thickened walls. All the larger arteries showed a thickened, calcified or hyalinated wall. This was particularly well shown in the van Gieson preparations; the vessels were tortuous, and their lumen was irregular on account of plaques of calcification. The intima of the larger vessels appeared festooned and often split from the media. Gitter cells, loaded with detritus, were often seen around the small vessels and capillaries in the perivascular spaces. It was in the deeper laminae and especially underneath the third layer that the vascularization was particularly increased. There were many holes where the vascular rings had fallen out or had shrunken and been drawn to the periphery. The parietal and especially the frontal cortex showed more marked vascular changes than the occipital cortex.

In general, the cortical lamination could be recognized, but this was not true throughout the whole cortex. In many sections and often in many places in the same section, especially those from the frontal cortex and to a lesser extent the parietal cortex, the third lamina had lost its cyto-architectural characteristics, and the differentiation between the third and deeper laminae became difficult. Another factor disturbing the normal architecture of the cortex was the occurrence of more or less widespread, irregular areas or clearings, in which very few or no nerve cells were left, these cells being replaced by a fibrous overgrowth of neuroglia and glia nuclei. These areas of devastation affected especially the third layer and were more prominent in the frontal cortex than in the parietal cortex. They were not

observed in sections from the occipital cortex. The perivascular gliosis in the shape of a clear area around the vessels, with a ring of pushed-away nerve cells, was frequently met with in sections from the frontal and parietal cortex.

The nerve cells were diminished in number. This was most obvious in the third layer. In general, one could recognize the three cellular zones of this layer, a small-cell outer zone, a medium-cell intermediate zone and a large cell inner zone, but in many places, especially in sections from the frontal cortex, the large pyramidal cells of the inner zone appeared so scarce and shrunken that this differentiation was difficult. A few cells in the first layer contained dark pigmented, light-refracting inclusions. There were other types of "Abbauprodukte" fairly constantly in the cortex and in the subcortical white matter, mostly around the blood vessels, but especially numerous around the vessels and underneath the pia of the insular cortex. These were round, homogeneous, stained blue with the Nissl method, nonrefracting bodies packed around the large arteries and increasing in number near the pia. Similar corpuscles were present around the sylvian aqueduct and underneath the midbrain meninges. These corpuscles looked like, and probably were, amyloid bodies.

The nerve cell changes in the cortex affected with distinct predilection the elements of the third layer (large-cell zone). In the occipital cortex many cells appeared to be normal—less in the parietal cortex. In the frontal cortex most of the cells were pathologically altered. These cells were atrophic, shrunken, some in a state of acute swelling, degenerated or completely destroyed, being replaced by glial clusters around their fragments. The shrinking of the cell bodies was a common and widespread form of cell change. Often, one found tremendously swollen cells with pale bodies and thick tortuous dendrites. Many cells of the third layer took the stain irregularly; some of them showed the Nissl bodies in clusters and many contained darkly stained fragments and corpuscles. Some cells showed actual karyolysis, the nuclei being broken up, fissured or split apart. Satellitosis was increased around these cells, and neuronophagic pictures were often observed.

Glial activity was distinctly increased in the cortex. The glia was hyperstainable; in one place, from a Nissl preparation of the parietal cortex, a blood vessel was cut slightly and the astrocytic glial lining of the vessel wall could be distinctly seen. Under a high power this perivascular glia appeared as a lacework of darkly stained fibrils and dark stellate glia cell bodies. In many places in the third layer of the frontal and parietal cortex, very large glia cells were found. Under a low power, they appeared as small vacuoles, but under a higher power one could see the large cell body, rich in protoplasm, with short and heavy prolongations and a small nucleus pushed to the periphery, and almost every one of these cells contained from one to three ganglion cells in a state of cytolysis. In the van Gieson preparations, the profuse secondary gliosis was well shown. Underneath the pia there was a marked degree of marginal gliosis, consisting of a thick network of glia fibrils but with few glia nuclei. In the white matter, on the yellow background of nerve fibers, one could see brown-pink, irregular patches of glia fibrils and numerous glia nuclei.

Spielmeyer's preparations for myelin sheaths did not show any actual demyelinization; however, under a high power one could see a moderate degree of myelin changes. The myelin sheaths along the nerve fibers were irregular, often bulging, heaped up into granules, sometimes broken into dark fragments, or retracted into clear droplets.

Basal Ganglia and Pedunculo-Hypothalamic Formations: The ependymal lining of the ventricular wall in some places appeared festooned. One observed under-

neath the ependyma a proliferation of a dense fibroglial network, with a heaping up of glia fibrils forming granules. The whole diencephalic region contained many amyloid bodies, already described. In some places one found regularly outlined pinholes of mucoid degeneration.

Vascularization of the whole region, including the peduncles, was much increased. The vessel walls were thick, calcified and often collected into groups and knots. The capillaries were intensely proliferated.

The nerve cell alterations were widespread and varied. Two types of alterations could be discriminated—acute or ischemic swelling, and chronic changes consisting

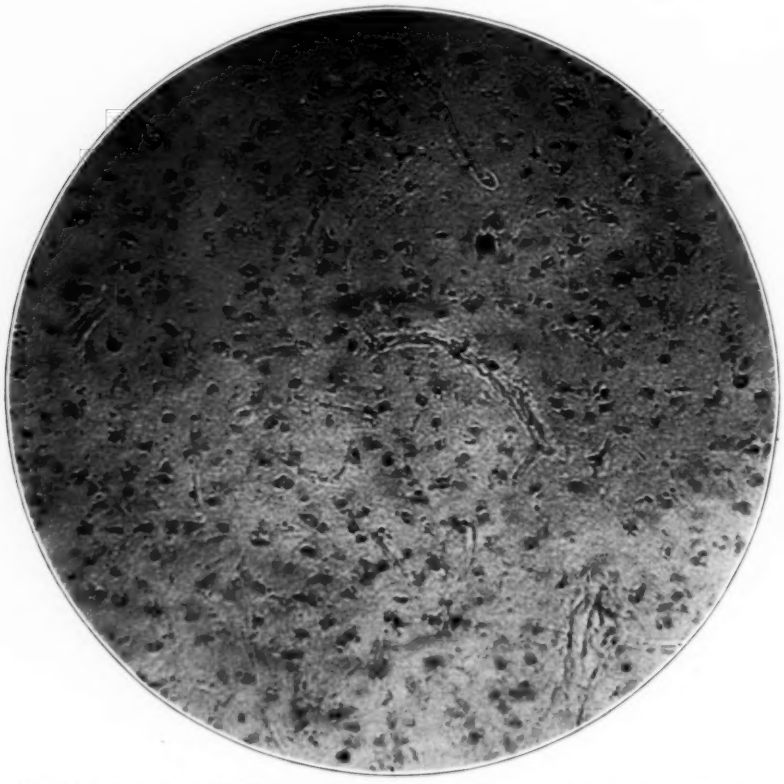

Fig. 5 (case 2).—Pallidum. The nerve cells are reduced in number; those remaining are shrunken and elongated and a few are swollen. The glia fibers without nuclei indicate regressive gliosis; Nissl methylene blue.

of reduction of the number of nerve cells, shrinking and hyperchromatosis. Secondary gliosis was so advanced in some places as to form an actual glial scar in this region. Thick, fibrous overgrowth with proliferation of glia nuclei, in some places, and without glia nuclei in others, differentiate the old lesions from the chronic but relatively recent and active processes (fig. 5). The formations of the diencephalic and pedunculo-hypothalamic regions were not equally degenerated. From this standpoint they could be divided into two groups: the thalamus, putamen and caudatum forming one relatively less affected group, and the pallidum, corpus luysii, substantia nigra and red nucleus the other more affected group.

Thalamus: The number of ganglion cells was not obviously diminished. All three principal nuclei that could be studied from sections in this region could be easily recognized, not only by their topography, but even from the characteristic cyto-architectural features. Vascularity was increased; capillaries were proliferated. A few zones of perivascular gliosis with disappearance of cells around the vessels could be seen. Most of the cells of the thalamus were in a state of acute degenerative change. Satellite cells were increased, and neuronophagic pictures were often met with. Some cells were completely destroyed; glial clusters were heaped up around their fragments. Swelling was more common, but shrinkage of cells was also observed. Many cells were filled with granular lipochrome pigment.

Putamen: Vascularity was much increased; capillaries were proliferated. The vessels had thickened walls, and about them were areas of degeneration with no nerve cells but increased glia nuclei. There were many small nerve cells fairly well preserved. Most of the cells, however, showed acute and chronic alterations, similar to those described in the thalamus. There were many amyloid bodies.

Nucleus Caudatus: This was the most affected of the three formations of the group under consideration. There was diminution of cells, and of those left only a few appeared to be in a good condition. The whole nucleus was largely replaced by thick-walled vessels and a great number of amyloid bodies.

Pallidum: Of the whole brain, the pallidum was the most affected. There were wide areas in which the nerve cells were literally swept out and replaced by dense, thick fibrous overgrowth, showing an advanced stage of secondary gliosis, with a less conspicuous increase of glia nuclei. Only a few small islands remained in which ganglion cells were found, and these were in a state of degeneration. This sclerotic state of the globus pallidus was obvious even macroscopically in Spielmeyer preparations by the pale, transparent appearance. The tremendous increase of thick vessels and capillaries, many holes with fallen out vessels and advanced perivascular gliosis completed the general picture of the lesion. The inner and intermediate segments were more affected than the outer segment. The nerve cells scattered in small islands showed eccentric nuclei with a black, sharply stained nucleolus. The cell bodies were irregular and greatly shrunken; the Nissl substance was diffused or collected in one corner of the cell body, while the rest was filled with granules of lipochrome pigment. Some cells were pale and swollen. Satellites and neuronophages were increased in number. Glia nuclei were numerous in these islands among the nerve cells. The small pallidal cells were not visible.

Corpus Luysii: The lesion of the corpus luysii came next in severity. Nerve cells were rarefied and dispersed in small islands among a dense fibroglial network. The nerve cells showed advanced alterations. There were shrinking hyperchromatosis and increased satellitosis. Many cells were pale and appeared as shadows, their nuclei being indistinct and their cell bodies crenated or actually spit. Many cells were in a state of lipochrome degeneration, filled with yellow granules. Not a single cell remained normal. Vascularization was much increased; the capillaries were proliferated.

Red Nucleus: This structure was small and had a sclerotic appearance on account of pronounced secondary gliosis. The number of cells was diminished. The chronic cell changes were obvious. Practically, not a single cell was normal. Vascularization was increased. There was a perivascular gliosis.

Substantia Nigra: This formation exhibited also a picture of an advanced secondary gliosis, especially around the vessels, and profound degenerative cell changes. The substantia nigra on frontal section consisted of groups of cells surrounded by clear fields of glia fibrils and nuclei. Most of the cells were in a state of pathologic alteration. Shrinking of cells was a most promi-

nent feature and usually affected the whole group. The nerve cells were small and shriveled up; many were broken or split. This last feature was met with nowhere else with such frequency as in the substantia nigra. Many cells contained yellow pigment collected in clusters and large fragments included in the vacuole. Many cells had lost their pigment and appeared pale. In other cells in a state of advanced cytolosis the pigment lay free near the fragments of the cell body and the nucleus. There were increased cytolysis and neuronophagia. Only a few cells appeared normal.

Spielmeyer preparations from the basal ganglia and pedunculo-hypothalamic regions showed moderate myelin sheath alterations similar to those described in the cortex. The ansa lenticularis did not show obvious demyelinization but appeared to be reduced in size. The pedunculo-hypothalamic bouquets formed by the fasciculus of Vicq d'Azyr, the fasciculus thalamicus and the fasciculus lenticularis were pale and slender. With small sections, not systematically cut in series, it was difficult to form an idea about the nerve fibers and tracts; no definite information was, therefore, at hand on this aspect of the pathology in the present case.

Cerebellum and Dentate Nucleus: These were involved in the same diffuse degenerative and atrophic process as the cortex and the basal ganglia, and in this case were involved in a relatively greater degree than the same structures in case 1. The Purkinje cells were much affected; there were many gaps and long stretches where no Purkinje cells remained; those that remained were degenerated, swollen, had a diffuse outline and were pale. In the dentate nucleus the number of cells was reduced; many cells were swollen. Scarlet red showed that the cells were loaded with fat granules. One Weigert section from the dentate nucleus showed that the nerve fibers composing the hilus were pale.

Spielmeyer preparations from the cerebellum and dentate nucleus showed obvious and marked myelin changes, swelling, beading and disintegration of myelin, especially in the fine fibers running out into the cortex and in the vicinity of the dentate nucleus.

Pons: The pontile cell groups appeared to be in a fair condition; a few were degenerated, especially in the fifth nucleus, where the cells were swollen and had eccentric nuclei. In the nucleus reticularis tegmenti many cells appeared shrunken, with granular protoplasm and broken up fragmented dendrites.

Medulla: One Weigert preparation from the medulla oblongata showed well developed olives with pale, discolored fibers composing its hilus. Weigert preparations from the pyramidal decussation did not show obvious degeneration of the fiber tracts.

Comment.—In this case, as in case 1, three components in the pathologic process affecting the brain can be discriminated: (1) primary chronic arteriosclerotic changes of the blood vessels; (2) chronic degenerative and atrophic changes in the nerve parenchyma with secondary gliosis as a direct reaction to the primary arteriosclerotic process, and (3) acute lesions: acute degenerative nerve cell alterations, acute swelling, ischemic cytolytic, karyolytic and chromatolytic changes, and edema.

From the standpoint of predominant localization of each of these three components, the last one was most diffuse, affecting practically the whole cerebrum. Perineural and perivascular edema and acute

ischemic cell changes can be explained from the clinical evidence of terminal uremia and death in coma.

The chronic sclerotic process of the blood vessels appears to be the primary cerebral lesion in this case. This was shown by both macroscopic and microscopic changes in the vessel walls of the brain and meninges. The primary nature of the vascular sclerotic process in the brain was supported by the clinical observation and by the history of the patient. The arteriosclerotic changes in the brain appeared to be especially prominent in the frontal cortex and in the basal ganglia. Macroscopically, one could observe the sclerotic state of the basilar vessels. Microscopic study showed a characteristic picture in the third layer of the cortex and in the pallidum: tremendous increase of thick-walled vessels and capillaries, advanced perivascular gliosis and many holes with the vascular ring fallen out or shrunken.

The pathologic process in the brain being primarily vascular, one can say that the chronic, degenerative and atrophic secondary changes observed in the nerve parenchyma were of a vasculotrophic nature, as has been described by Spielmeyer [7] in cerebral arteriosclerosis. Disturbances in the blood supply, a state of chronic ischemia, probably play the principal rôle in causing the shrinking, atrophy and eventual breaking down of the nerve cells. This secondary chronic degenerative process, which followed the primary vascular arteriosclerotic process, showed the same topographic distribution as the latter — the frontal cortex (third layer) and the basal ganglia (pallidum and pedunculohypothalamic formations) being the most affected regions of the brain.

The glial reaction further substantiates the contention that the secondary degenerative process in its evolution was one of long duration. Two types of glial reaction could be discriminated: (1) "Regressive" gliosis consisting mostly of a dense fibrous overgrowth without increase in number of glia nuclei and indicative of an old lesion (neuroglial sclerosis of the pallidum, marginal gliosis, subependymal gliosis). (2) "Progressive" gliosis characterized by proliferation of glia nuclei, many of them showing active division, hyperstainable glia cells and fibrils, glial clusters, indicative of an active glial reaction where the lesion was relatively recent. Topographically, this was a most diffuse feature observed in the cortex, striatum and cerebellum.

On the whole, the histopathology observed in this case closely resembles that described by Foix and Nicolesco [8] in Parkinson's disease:

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7. Spielmeyer, W.: Vasomotorisch trophische Veränderungen bei zerebraler Arteriosclerose, Monatschr. f. Psychiat. u. Neurol. **68**:605, 1928; Histopathologie des Nervensystems, Berlin, Julius Springer, 1922.

8. Foix, C., and Nicolesco, A.: La maladie de Parkinson, in les noyaux gris centraux et la région mesencéphalo sous optique, Paris, Masson & Cie, 1925.

atrophic sclerotic changes in the frontal cortex, progressive and regressive glial reaction, multiple foci of cellular disintegration, and increase of lipochrome pigment, dropping out, shrinking, karolytic and cytolytic changes in the nerve cells of the basal ganglia, especially in the pallidum, corpus luysii and substantia nigra.

GENERAL COMMENT

These two cases, clinically, seem entirely different; however, both show the same essential features: epilepsy and the symptomatologic pattern of neurosomatic deterioration. In case 1, that of a child, deterioration developed more rapidly and was more destructive, leading in nine years to profound dementia and cerebral flexion paraplegia. In case 2, that of a man 65 years of age, with late epilepsy, the neurologic picture essentially characteristic of neurosomatic deterioration developed more slowly and was not so dramatic, and the symptomatologic pattern was one that may be identified with arteriosclerotic parkinsonism.

Pathologically, in both cases, evidence was found of a primary vascular cerebral lesion which in case 1 was an acute inflammatory lesion—meningo-encephalitis; in case 2, on the contrary, a chronic and noninflammatory lesion—cerebral arteriosclerosis. In both cases the primary vascular lesion was the starting point of a chronic degenerative and atrophic process affecting principally the frontal cortex and basal ganglia. The cortex showed a more widespread lesion in case 1; on the contrary, the pallidum was relatively more degenerated and sclerotic in case 2. In spite of the fact that the clinical picture was distinctly more advanced and severe in case 1 than in case 2, the corrseponding degree of severity of pathologic changes in the respective cases could not be established. One must bear in mind that the lesion in case 1, whatever its nature and degree of severity, occurred in a critical period of life before puberty, and for that reason this lesion was potentially more destructive to cerebral function. In case 1, the degenerative pathologic process was of an active subacute character, showing a predominance of the "progressive" glial reaction, while this process in case 2 was of a more chronic, sclerotic type, showing mostly the fibroglial secondary reaction of a "regressive" variety (glial scar).

In both of the cases reported, in spite of a great diffusion of the cerebral lesions, not only did the frontal cortex, pallidum and pedunculo-hypothalamic formations—corpus luysii, substantia nigra and red nucleus —show more profound alterations, but, what is particularly important, the alterations in these areas of the brain — the pallidum especially — were those of a chronic degenerative and atrophic process. This process, apparently secondary to the primary cerebral lesion, appears to represent in a plausible fashion the pathologic foundation of the evolution and of

the symptomatology of neurosomatic deterioration. Following the prevalent idea, one may refer dementia to lesions of the cerebral cortex and rigidity to a lesion of the basal ganglia and midbrain; however, the progressive dementia and rigidity observed in the course of neurosomatic deterioration of persons with epilepsy, in our minds, are a sum total of both cortical and subcortical pathologic changes. These two essential clinical components of deterioration represent merely two aspects, one psychic, the other motor, of one clinicopathologic syndrome reflecting probably a progressive degeneration of a complex frontopallidomesencephalic system.

The particular syndrome and the pathologic process described in our cases are not unfamiliar to those who happen to practice their observations in that clinical field which truly can be called "the dumping ground of neurology."

Foerster,[9] under the name of "congenital pallidal rigidity," described a number of cases that were characterized by a syndrome consisting of epilepsy from infancy, imbecility or idiocy and progressive rigidity; as in some cases pyramidal symptoms developed in the further evolution of the condition, he called the whole symptom complex a "pyramidopallidal syndrome." This author's classic paper on the extrapyramidal disorders of motiltiy[10] opens with a record of such a case. The case history and clinical photographs illustrating it do not leave any doubt as to the identity of the syndrome with that developing in many persons with epilepsy in the course of deterioration, regardless of the origin and of the age of onset of epilepsy[1]: generalized rigidity, flexion attitude of the head, trunk and extremities, flexion contracture of the lower extremities; these are shown distinctly in Foerster's illustrations.

Bielschowsky,[11] in a clinicopathologic study, under the name of "progressive rigidity" described the case of a boy who at 6 years of age, following an acute illness, developed chorea; later, progressive muscular rigidity set in; the choreic movements, little by little, became extinguished; eventually, flexion contractures of the lower extremities developed; the patient became permanently bedridden in a clasp-knife attitude; speech and swallowing became greatly impaired; there were associated epileptic attacks and profound dementia; the patient died at 14 years of age. A pathologic study showed atrophic and degenerative lesions in the brain, with advanced secondary gliosis. The third layer of

9. Foerster, O., quoted by Gareiso, A., and Marotta, A.: La rigidité congénitale régressive, Syndrome de Mme. Cecile Vogt (état marbré du corps strié), Arch. de méd. d. enf. **31**:197 (April); 276 (May) 1928.

10. Foerster, O.: Zur Analyse und Pathophysiologie der striären Bewegung-Störungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:1, 1921.

11. Bielschowsky, M.: Weitere Bemerkungen zur normalen und pathologischen Histologie des Striärensystems, J. f. Psychol. u. Neurol. **27**:233 (May) 1922.

the frontal cortex and the basal ganglia were the most affected; in the latter the most prominent lesions were in the corpus striatum. In the pallidum and pedunculo-hypothalamic formations, corpus luysii and substantia nigra, the lesions were not so advanced, although quite severe and probably of later date. Bielschowsky attributed the chorea to the lesion in the striatum and the progressive rigidity, which developed later, to the later lesion in the pallidum and substantia nigra.

Similar observations of rigidity with dementia and eventual development of flexion contractures in the lower extremities were reported by Urechia and Nicolesco, Babonneix and Lance, Filimonoff and Onato (quoted by Gareiso and Marotta).[9] In most of these observations, epileptic attacks were recorded. One case of Urechia and Nicolesco was that of a girl aged 17, who at 2 years of age, following an encephalitis, developed at first chorea, then progressive rigidity and myoclonic movements; she had epileptic attacks, became mentally deficient, and could not talk; pathologically, there were found lesions in the striatum and pallidum, in the corpus luysii and substantia innominata (Reichert's), in the nucleus dentatus and in the nucleus of the vagus.

In a study of myoclonus in persons with epilepsy,[12] we were able to show by a survey of the literature that in most cases of myoclonus associated with epilepsy and deterioration extrapyramidal symptoms were present, and the pathologic study of the central nervous system in most cases showed lesions in the basal ganglia, the pallidum and substantia nigra often being particularly affected. Lesions of the dentate nucleus were found constantly. On the contrary, in cases of myoclonus free from epilepsy, deterioration was not present, the akineto-hypertonic symptom complex was not observed, and the lesions in the central nervous system were confined to the cerebellum and dentate nucleus, while the basal ganglia were intact. On the grounds of this study, we have advanced the view that the myoclonic components in the myoclono-epileptic cases are referable to involvement of the dentate system (a cerebellotropic or dentatotropic lesion), while the epileptic component (deterioration) in such cases is reflected mostly in the diencephalotropic degenerative lesion of the brain.

Thus, it seems that the broad clinical syndrome, consisting of a chronic convulsive state with progressive dementia and progressive rigidity, in many cases is associated with a degenerative process, of diffuse distribution in the brain, but with particularly profound and elective lesions in the frontal lobes (third cortical layer), basal ganglia (pallidum) and midbrain (substantia nigra and red nuclei).

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12. Hodskins, M. B., and Yakovlev, P. I.: Anatomico-Clinical Observations on Myoclonus in Epileptics and on Related Symptom Complexes, Am. J. Psychiat. **9**:827 (March) 1930.

Reference should be made also to the pathologic alterations in the viscera. In case 1, the liver was distinctly under weight, small and sclerotic, with a thick adherent capsule, proliferation of connective tissue and degenerative changes in the liver cells with vacuolization. In case 2, histologic study of the liver was not made, but on macroscopic examination it appeared small and sclerotic, gray, hard and finely nodulated, and the capsule was adherent.

In connection with these visceral changes it is of interest to mention the observation of Guiraud [13] in a case similar to our case 1: A boy, aged 2½, was taken ill with fever and convulsions; following this he showed an arrest of mental development; he had frequent epileptic attacks — from ten to forty a day; besides epileptic attacks, which continued until death, he developed "parkinsonian symptoms": fixed facies, flexion attitude of the body and bilateral muscular rigidity, more pronounced on the right side. The patient died at 17 years of age from pulmonary tuberculosis. Histologic examination of the central nervous system showed slight thickening of the pia, rarefaction of the pyramidal cells and areas of neuroglial sclerosis in the cortex. The putamen and nucleus caudatus showed areas of disintegration around the vessels. The cells of the globus pallidus were atrophied, and many were missing. In the medulla and pons there were foci of intense perivascular reaction with plasmocytes and lymphocytes. The substantia nigra was also the seat of perivascular infiltration, but especially of nerve cell lesions, which were much more intense than in other parts of the brain.

The liver was studied particularly. Macroscopically, it was rather hypertrophied (1,500 Gm. at 17 years of age); it was hard and granular in appearance, filled with small parenchymatous nodules that were scarcely visible to the naked eye and buried in a mass of connective tissue. Histologically, there were proliferation of connective tissue and cellular cirrhosis; the hepatic cells were degenerated and showed a particular cystic transformation of the nuclei.

Guiraud compared his case with a group of cases presenting the pathologic syndrome of hepatolenticular degeneration and called the condition described by him "syndrome hépato-encéphalique."

We shall refer also to the observations of Myerson,[14] Thom,[15] and the more recent studies of Patterson and Weingrow [16] on the relation

13. Guiraud, P.: Syndrome hépato-encéphalique, Encéphale **26**:277 (April) 1928.

14. Myerson, A., quoted from Patterson, H. A., and Weingrow, S. M.: J. Nerv. & Ment. Dis. **41**:444 (July) 1914.

15. Thom, D. A., quoted from Patterson, H. A., and Weingrow, S. M.: J. Nerv. & Ment. Dis. **43**:422 (May) 1916.

16. Patterson, H. A., and Weingrow, S. M.: The Relation Between Brain and Liver Weights in Epilepsy Considered from Standpoint of Onset and Duration in About 200 Cases, Psychiat. Quart. **2**:171 (April) 1928.

between brain and liver weights in persons with epilepsy. These authors demonstrated from a survey of a large number of autopsy records that the liver in persons with epilepsy in nearly 70 per cent of cases was smaller and lighter than in the normal weight relations between the liver and brain.

These visceral changes, coinciding with the lesions in the central nervous system, are, of course, of fundamental importance and deserve the attention of thoughful investigators. We believe that the lesions of the liver, pancreas and suprarenals, as were found in our case 1, were not merely coincidental; they can be looked on as visceral components of the pathology of neurosomatic deterioration.

We wish to emphasize that in the present as well as in previous publications [17] on the clinical symptoms and pathology of neurosomatic deterioration, we were not concerned with finding the "etiology" or the "pathogenesis" of epilepsy as such, but with the clinical and pathologic aspects of the various disease processes in the central nervous system, of which epilepsy is one of the most constant and usually one of the earliest manifestations. In other words, it is not "the cause of things" but "the things caused" (Hughlings Jackson) that was the main idea in our observations. It is with this idea in mind that we are reporting the clinicopathologic study in these two cases.

Being rather limited in our technical means, we could not make as complete a detailed histopathologic study of the two brains as they deserved. The study of glial reactions, the microchemical study of various "Abbauprodukte," as well as a systematic study of nerve fibers and tracts were not made. This is a serious gap, which we fully realize; however, the few methods used, especially those of Nissl and van Gieson, gave us a fairly representative general picture of the nature and distribution of the pathologic changes and justify the reporting of the results of our observations.

SUMMARY

Two cases are reported, one of epilepsy following encephalitis in early childhood, the other of late epilepsy with cerebral arteriosclerosis and cardiorenal disease. Both cases presented the characteristic clinical picture of progressive neurosomatic deterioration. The first was an advanced stage of deterioration, with generalized muscular rigidity, more marked in the lower extremities, clasp-knife attitude of the body (cerebral flexion paraplegia), pseudobulbar symptoms and profound dementia. In case 2 the dementia was less pronounced and the neurologic condition was identical with the akineto-hypertonic syndrome of arteriosclerotic parkinsonism. Pathologic study of the central nervous

17. Hodskins and Yakovlev (footnotes 1 and 12).

system in both cases showed a diffuse involvement of the brain by acute and chronic degenerative changes. The chronic changes in case 1 were attributed to an inflammatory lesion (encephalitis), and in case 2 to arteriosclerosis. In both cases the chronic degenerative and atrophic lesions affected especially the frontal cortex (third layer), basal ganglia (pallidum) and pedunculo-hypothalamic formations (corpus luysii, substantia nigra and red nucleus). These chronic degenerative changes were considered as representing the pathology of neurosomatic deterioration in the two cases reported. It was suggested that the degeneration of the complex frontopallidomesencephalic system of the brain clinically is expressed by a progressive psychomotor syndrome consisting of a chronic convulsive state, dementia and rigidity, eventually leading to a cerebral flexion paraplegia (flexion contractures, clasp-knife attitude and pseudobulbar symptoms).

The chronic changes in the visceral organs, especially in the liver, may be considered as the visceral component of the pathology of neurosomatic deterioration.

THE EPILEPTIC CONVULSIONS OF DEMENTIA PARALYTICA

THEIR RELATION TO SCLEROSIS OF THE CORNU AMMONIS *

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Considerable interest has been manifested recently in vascular spasms [1] and their relation to cerebral lesions and to the convulsions of epilepsy. There have been numerous observations at operations that epileptic convulsions are accompanied by blanching of the brain,[2] and recently Gildea and Cobb [3] have reported convulsions in cats in which they produced anemia of the brain by tying the large vessels in the neck. It was therefore thought that if in dementia paralytica, which frequently shows epileptic convulsions as a symptom, any evidence of such vascular spasms could be found, the relation of this to the incidence of convulsions in the patients would be very significant. It was for this reason, at the suggestion of Dr. Spielmeyer, that I undertook to study the cases of dementia paralytica in the Deutsche Forschungsanstalt in Munich.

Sclerosis of the cornu ammonis was first described in 1825 by Bouchet and Cazauvieilh; [4] since then the cause of this sclerosis and its relation to epileptic convulsions have been much debated because it has been found in numerous unrelated diseases and in cases in which there

* Submitted for publication, June 10, 1931.

* From the Deutsche Forschungsanstalt für Psychiatrie (Kaiser Wilhelm Institute).

1. Spielmeyer, W.: Die Pathogenese des epileptischen Krampfes, Ztschr. f. d. ges. Neurol. u. Psychiat. **109**:501, 1927; Zur Einführung: Die anatomische Krankheitsforschungs in der Psychiatrie, in Bumke: Handbuch des Geisteskrankheiten, Berlin, Julius Springer, 1930, vol. 11, pt. VII. Neubürger, K.: Ueber streifenförmige Erkrankungen der Grosshirnrinde bei Arteriosklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **101**:452, 1926. de Vries, E.: Acute Diseases of the Brain Due to Functional Disturbance of the Circulation, Arch. Neurol. & Psychiat. **25**:227 (Feb.) 1931.

2. Penfield, W.: The Place of Neurosurgery in the Treatment for Epilepsy, Arch. Neurol. & Psychiat. **24**:652 (Sept.) 1930. Foerster, O.: Hyperventilation Epilepsie, Zentralbl. f. d. ges. Neurol. u. Psychiat. **38**:289, 1924. Kennedy, Foster: Epilepsy and the Convulsive State, Arch. Neurol. & Psychiat. **9**:567 (May) 1923.

3. Gildea, E. F., and Cobb, S.: The Effects of Anemia on the Cerebral Cortex of the Cat, Arch. Neurol. & Psychiat. **23**:876 (May) 1930.

4. Bouchet, C., and Cazauvieilh, J. B.: De l'épilepsie considérée dans ses rapports avec l'aliénation mentale, Paris, Migneret, 1825.

have been no convulsions. It has been reported in general in three types of diseases: (1) those in which there is an organic obstruction of the lumen of the blood vessels, such as occurs in arteriosclerosis,[5] septic emboli,[6] fat embolism,[7] etc.; (2) those with inflammatory changes in the brain, such as cerebral syphilis,[5] dementia paralytica,[8] tuberculous [9] and other meningitides,[10] and epidemic encephalitis; [5] (3) those without organic vascular or inflammatory lesions, such as carbon monoxide poisoning,[11] morphine poisoning,[12] whooping cough,[13] eclampsia,[14] brain trauma,[15] idiocy,[5] cerebral infantile hemiplegia [5] and idiopathic epilepsy.[16]

Convulsions are known to occur in all of the diseases in the three groups mentioned, and practically all of the cases reported were accom-

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5. Spielmeyer, W.: Zur Pathogenese örtlich elektiver Gehirnveränderungen, Ztschr. f. d. ges. Neurol. u. Psychiat. **99**:756, 1925. Uchimura, J.: Zur Pathogenese der örtlich elektiver Ammonshornerkrankung, Ztschr. f. d. ges. Neurol. u. Psychiat. **114**:567, 1928.

6. Löwenberg, K.: Ueber gefäss-bedingte Herde im Ammonshorn, J. f. Psychol. u. Neurol. **39**:1, 1929.

7. Neubürger, K.: Ueber cerebrale Fett und Luftembolie, Ztschr. f. d. ges. Neurol. u. Psychiat. **95**:278, 1925.

8. Bratz, E.: Ueber das Ammonshorn bei Epileptischen und Paralytikern, Allg. Ztschr. f. Psychiat. **56**:841, 1899; Das Ammonshorn bei Epileptischen, Paralytikern, Senildementen und anderen Hirnkranken, Monatschr. f. Psychiat. u. Neurol. **47**:56, 1920; Ueber Ammonshornsklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **81**:45, 1923. Pfleger, L.: Beobachtungen über Schrumpfung und Sclerose des Ammonshornes bei Epilepsie, Allg. Ztschr. f. Psychiat. **36**:359, 1880. Alzheimer, A.: Histologische Studien zur Differentialdiagnose der progressiven Paralyse, Jena, 1904. Borosdin, Rosenstein and Ljubimow, quoted by Steiner: Arch. f. Psychiat. **46**:1091, 1910. Taft, A.: The Incidence of Sclerosis of the Cornu Ammonis and Convulsions in General Paresis, J. Neurol. **2**:221, 1921. Jelliffe and White: Diseases of the Nervous System, Philadelphia, Lea & Febiger, 1929. Spielmeyer (footnote 5).

9. Bodechtel, G., and Opolski, A.: Gefässbedingte Herde bei der tuberkulösen Meningitis, Ztschr. f. d. ges. Neurol. u. Psychiat. **125**:401, 1930.

10. Wertham, Frederic: The Cerebral Lesions of Purulent Meningitis, Arch. Neurol. & Psychiat. **26**:549 (Sept.) 1931.

11. Meyer, A.: Ueber die Wirkung der Kohlenoxydvergiftung auf des Zentral-Nervensystem, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:201, 1925.

12. Weimann, W.: Gehirnveränderungen bei akuter und chronischer Morphin-Vergiftung, Ztschr. f. d. ges. Neurol. u. Psychiat. **105**:704, 1926.

13. Neubürger, K.: Ueber die Pathogenese der Keuchhusten Eklampsie, Klin. Wchnschr. **3**:113, 1925.

14. von Braunmühl, A.: Ueber Gehirnveränderungen bei puerperaler Eklampsie und ihre Entstehung durch Kreislaufstörung, Ztschr. f. d. ges. Neurol. u. Psychiat. **117**:698, 1928.

15. Neubürger, K.: Akute Ammonshornveränderungen nach frischen Hirnschussverletzungen, Krankheitsforschung **7**:219, 1929.

16. Footnotes 4, 5 and 8.

panied clinically by convulsions except in some of those produced by organic vascular lesions; it is to Spielmeyer [17] that credit belongs for an explanation of the cause of sclerosis of the cornu ammonis in these various conditions. He showed that the lesion is essentially the same in all cases; since the sclerotic area is always in the territory supplied by one blood vessel, he concluded that it is due to a disturbance of the blood supply to this area. In cases in which there was no organic occlusion of the vessel, he stated that the lesion must be due to a functional disturbance of the circulation (vascular spasm); he showed that in many cases in which the patients died shortly after convulsions fresh changes could be found in the ganglion cells of Sommer's sector which are exactly similar to those found immediately after vascular lesions elsewhere in the brain—"ischaemische Zellveränderungen." [18] He has followed the changes in the cornu ammonis from such fresh ischemic changes to advanced sclerosis, and he stated that a vascular spasm of a sufficiently long duration can cause these changes; he denied that there must necessarily be a paralysis of the vessel wall, as has been claimed by other workers. He stated that the vascular spasm, which is the result of some influence on the innervation of the cerebral vessels, is a link in the chain of events in the epileptic convulsion.

The existence of an innervation of cortical blood vessels has recently been conclusively demonstrated by Penfield.[19] Forbes and Wolff [20] have reviewed the earlier literature on this subject, and in beautifully controlled observations of the pial vessels through a window in the skull of dogs they noted contraction of these vessels on stimulation of the cervical sympathetics and dilatation of the vessels on stimulation of the vagus. Spielmeyer's explanation of the vascular origin of sclerosis of the cornu ammonis is supported by the studies on the blood supply of this region by Uchimura,[5] who showed that Sommer's sector, which is always most severely injured, is supplied by one long artery, while the dorsal band, which in most cases is spared, has several small nutrient arteries. Objections [21] have been raised to the theory that the severe

17. Spielmeyer, W.: Das Interesse am Studium der Kreislaufstörungen im Gehirn und die Paralyse-Anatomie, Wien. klin. Wchnschr. **41**:1011, 1928; footnote 5.

18. Spielmeyer, W.: Histopathologie des Nervensystems, Berlin, Julius Springer, 1922.

19. Penfield, W. G.: Intracerebral Vascular Nerves, Arch. Neurol. & Psychiat., to be published.

20. Forbes, H. S., and Wolff, H. G.: Cerebral Circulation: III. The Vasomotor Control of Cerebral Vessels, Arch. Neurol. & Psychiat. **19**:1057 (June) 1928.

21. Shimoda, M.: Einige Beiträge zur Histopathologie des Gehirns, Monatschr. f. Psychiat. u. Neurol. **74**:65, 1930.

ischemic cell changes found in acute cases may be due to a short temporary occlusion of the circulation, but it has been shown recently by Gildea and Cobb [3] that stoppage of the cerebral blood supply for even very short intervals results in permanent cell injury.

With the foregoing considerations in mind, an attempt was made to study from clinical and anatomic points of view cases of dementia paralytica that showed a sclerosis or fresh, ischemic, ganglion-cell changes in the cornu ammonis. Thirty-four cases with such lesions in the cornu ammonis were found. This number would probably have been greater if sections had been made from both cornua ammonis of all cases of dementia paralytica at the Deutsche Forschungsanstalt, but it has been the custom here to cut sections from only one cornu ammonis; our observations and those of others indicate that the sclerosis, when present, is usually unilateral.

In thirty of the thirty-four cases it was possible to obtain a clinical history; only these thirty were included in this study.

A brief summary of the thirty cases will be given later. It appears unnecessary to give details of the clinical history and pathologic examinations in these cases. All the cases were diagnosed clinically as dementia paralytica on the basis of the anamnesis, and of neurologic and serologic observations. Pathologically, they all presented the typical appearance of dementia paralytica, with such additional changes as will be noted. Iron was found in all cases in which the macroscopic or microscopic tests [22] were made. The complete records were obtained from the various hospitals in which the patients had been treated, and the majority were fairly satisfactory. It is considered unnecessary here to describe the variations in the extent of the lesions found in the cornu ammonis, as all conformed to the various types described by Bodechtel,[23] who explained the differences on the basis of individual variations in the vascular supply of this region. The term epileptic convulsions is used here without regard to the severity or duration of the period of unconsciousness or of the convulsive movements. Such facts were difficult to determine in some cases, as the records contained such terms as "schwere paralytische Anfälle, leichte paralytische Anfälle, status epilepticus," etc., without further explanations, but it was possible to determine in practically all cases whether or not the attacks were accompanied by convulsive movements and unconsciousness.

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22. Spatz, H.: Ueber eine einfache Methode zur anatomischen schnell Diagnose der progressiven Paralyse, München. med. Wchnschr. **69**:1376, 1922.

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REPORT OF CASES

CASE 1.—A. B., a man, aged 43, the onset of whose illness was at the age of 35, was admitted to the Psychiatrische Klinik, Munich, on July 27, 1923, three years after the onset. He was transferred to the Heil und Pflegeanstalt, Eglfing, on Sept. 10, 1925, and was given fever therapy (nucleic acid), arsphenamine and mercury. He had numerous minor and major epileptic attacks from the time of entry until one week before death, on May 31, 1930. Necropsy showed edema of the lungs, old pleurisy and macroscopic evidence of dementia paralytica. Microscopically, the brain showed signs typical of dementia paralytica and sclerosis of the cornu ammonis.

CASE 2.—E. B., a woman, aged 55, the onset of whose illness was at the age of 50, was admitted to the Psychiatrische Klinik, Munich, on Nov. 17, 1924, and was transferred to the Heil und Pflegeanstalt, Eglfing, on March 30, 1925. The patient had numerous epileptic attacks during the last month of life and died in status epilepticus. No records of the treatment given or of the necropsy were available. Microscopic sections of the brain showed signs typical of dementia paralytica and sclerosis of the cornu ammonis.

CASE 3.—K. G., a man, aged 50, the onset of whose illness was at the age of 49, was admitted to the Psychiatrische Klinik, Munich, on Aug. 17, 1925. He was treated with malarial fever and afterward transferred to the Heil und Pflegeanstalt, Eglfing, on March 18, 1926. The patient had epileptic convulsions one week before admission to the Psychiatrische Klinik and at intervals until death, which occurred thirty-six hours after a prolonged status epilepticus. Necropsy showed gangrenous cavities and multiple small abscesses in the right lung, fresh embolic abscesses in the right kidney, septic hemorrhages in the left suprarenal gland and in the meninges, decubitus and syphilitic aortitis. Microscopic examination of the brain showed signs typical of dementia paralytica, sclerosis of the cornu ammonis, metastatic septic lesions composed chiefly of polymorphonuclear cells scattered throughout the cortex and septic thrombi in the meningeal vessels.

CASE 4.—K. L., a man, aged 46, the onset of whose illness was at the age of 42, was admitted to the Psychiatrische Klinik, Munich, on July 7, 1925. The patient had previously received malarial therapy twice at the Schwabinger Krankenhaus. He was transferred to the Heil und Pflegeanstalt, Eglfing, on Sept. 19, 1925, and died in epileptic convulsions on Aug. 28, 1927, without any previous record of convulsions. Necropsy showed hypostatic pneumonia, fresh tuberculous lesions in the left lung, cystitis and pyelitis, hypertrophy of the left side of the heart and macroscopic evidence of dementia paralytica in the brain. Microscopically, the brain showed signs of dementia paralytica in the so-called stationary stage, i. e., the infiltration of the meninges and cerebral blood vessels was very slight, and fresh cell changes were not marked, with the exception that the ganglion cells in Sommer's sectors and the end-plate of the cornu ammonis showed ischemic changes, and numerous "Gliastrauchwerk" were found in the cerebellum. In view of the slight degree of inflammatory reaction present, iron stains were made to confirm the anatomic diagnosis, and moderate quantities of iron were present in the walls of the blood vessels and in the Hortega cells of the cortex.

CASE 5.—B. W., a woman, aged 40, the onset of whose illness was at the age of 37, was admitted to the Psychiatrische Klinik, Munich, on March 20, 1923, and transferred to the Heil und Pflegeanstalt, Eglfing, on April 4, 1926. No mention of the mode of therapy was found in the case history. She had numerous

epileptic convulsions from April 4, 1926, until a few days before death on Oct. 11, 1926. Autopsy showed extreme emaciation, marked atrophy of the internal organs, multiple abscesses of the lungs (aspiration pneumonia), chronic cystitis, ureteritis, pyelonephritis and macroscopic evidences of dementia paralytica in the brain. Microscopically, the brain showed signs typical of dementia paralytica and sclerosis of the cornu ammonis on both sides.

Case 6.—M. P., a man, aged 51, the onset of whose illness was at the age of 47, was admitted to the Psychiatrische Klinik, Munich, on Dec. 2, 1922, and transferred to the Heil und Pflegeanstalt, Eglfing, on July 12, 1922. The onset of the illness was with epileptic convulsions on May 23, 1922, and the patient had numerous convulsions at intervals until one month before death on Nov. 10, 1926. Necropsy showed advanced syphilitic aortitis, subchronic tuberculosis of the upper lobes of the lungs, fresh miliary tuberculosis of the lower lobes, tuberculosis of the mediastinal lymph nodes, chronic cystitis, fresh anemic infarcts of the spleen, decubital ulcers and macroscopic evidence of dementia paralytica in the brain. Microscopically, the brain showed the typical changes of dementia paralytica and sclerosis of the cornu ammonis.

Case 7.—E. M., a boy, aged 16, the onset of whose illness was at the age of 10, was admitted to the Psychiatrische Klinik, Munich, on Feb. 21, 1922, and inoculated with recurrent fever. He was released from the Psychiatrische Klinik on June 31, 1922, and was admitted to the Heil und Pflegeanstalt, Haar, on Nov. 13, 1922. The first epileptic convulsion occurred in December, 1926, after which he had numerous convulsions until Sept. 14, 1927. He died on April 17, 1928. Necropsy showed verrucose endocarditis, tuberculosis of the hilar lymph nodes, thrombosis of all the cerebral sinuses and fresh hemorrhages in the right hemisphere. Microscopically, the brain showed signs typical of Lissauer's dementia paralytica, and in the occipital lobe there were numerous small fresh hemorrhages into the atrophic cortex. Many of the pial vessels were filled with thrombi. There was a sclerosis of many lobules of the cerebellum.

Case 8.—T. G., a woman, aged 33, the onset of whose illness was at the age of 29, was admitted to the Psychiatrische Klinik, Munich, on Feb. 5, 1923, and was transferred to the Heil und Pflegeanstalt, Eglfing, on March 6, 1923. She was treated with arsphenamine and mercury. She had numerous epileptic convulsions in the period from Sept. 3, 1923, to March, 1927, and was free from them until death on June 6, 1927. Necropsy showed subchronic tuberculosis of the lungs and of the hilar lymph nodes, chronic cystitis and pyelitis, and atrophy of the internal organs. Examination of the brain showed signs typical of dementia paralytica, sclerosis of the cornu ammonis on one side and fresh ischemic changes in the ganglion cells of Sommer's sector on the other side. One small meningeal vessel on the dorsolateral surface of the medulla showed typical Heubner's endarteritis.

Case 9.—A. S., a woman, aged 19, the onset of whose illness was at the age of 16, was admitted to the Heil und Pflegeanstalt bei Konstanz, in March, 1929, and treated with malarial fever. The patient had numerous convulsions in the period from Sept. 28 to Oct. 5, 1930, after which she was unconscious until death on October 7. No record of the autopsy was available except the macroscopic description of the brain, which was markedly atrophic; all the cerebral sinuses were thrombosed. Microscopically, the brain showed signs of dementia paralytica and numerous small fresh hemorrhages in the cortex and white matter of the brain, particularly in the right occipital lobe. Numerous pial vessels were filled

with thrombi. The ganglion cells in Sommer's sector and in the end-plate of the cornu ammonis on the right side showed fresh ischemic changes.

Case 10.—O. Z., a man, aged 30, the onset of whose illness was at the age of 25, was first admitted to the Psychiatrische Klinik, Munich, on Aug. 15, 1922, and was treated with malarial fever, arsphenamine and mercury. After two short remissions he was committed to the Heil und Pflegeanstalt, Haar, on Feb. 9, 1925. He had numerous epileptic convulsions from August, 1922, until a few days before death on Sept. 14, 1927, of bronchopneumonia. No record of the autopsy report was available. Microscopically, the brain showed the changes typical of dementia paralytica and sclerosis of the cornu ammonis.

Case 11.—J. T., a man, aged 22, the onset of whose illness was at the age of 13, was first admitted to the Psychiatrische Klinik, Munich, on July 27, 1920, and released on July 30. He was readmitted on Nov. 30, 1925, and transferred to the Heil und Pflegeanstalt, Eglfing, on Jan. 13, 1926. He was treated with arsphenamine and mercury. The patient had petit mal and convulsive attacks at intervals from 1920 until death in status epilepticus on Aug. 13, 1927. Necropsy showed aspiration pneumonia, fresh tuberculosis of the lungs and bronchial lymph nodes, pyelitis, pyelonephritis, hemorrhagic cystitis and macroscopic evidence of dementia paralytica in the brain. Microscopically, the brain showed signs typical of dementia paralytica, an apparently fresh sclerosis of the cornu ammonis and loss of cells in the molecular layer of the cerebellum in several lobes.

Case 12.—J. S., a man, aged 53, the onset of whose illness was at the age of 52, was admitted to the Psychiatrische Klinik, Munich, on April 16, 1926, and died on the following day in status epilepticus. He had received treatment ten years previously for venereal disease. He had had several convulsions in the three weeks preceding admission to the Klinik. No record of the necropsy observations was available. Microscopic examination of the brain showed signs typical of dementia paralytica and sclerosis of the cornu ammonis.

Case 13.—L. W., a man, aged 39, the onset of whose illness was at the age of 29, was admitted to the Psychiatrische Klinik, Munich, on April 20, 1926, and was inoculated twice with malaria but without any febrile reaction. He had numerous convulsions on the two days preceding death and died in status epilepticus on Nov. 14, 1927. No record of the necropsy observations was available. Microscopically, the brain showed signs typical of dementia paralytica and sclerosis of the cornu ammonis.

Case 14.—R. H., a man, aged 43, the onset of whose illness was at the age of 42, was given malarial and arsphenamine therapy at home, and was admitted to the Psychiatrische Klinik, Munich, on March 10, 1924. He had numerous epileptic attacks from January to September, 1923, with no further mention of convulsions from then until death in April, 1924. No record of the necropsy observations was available. Microscopically, the brain showed the changes of dementia paralytica and sclerosis of the cornu ammonis.

Case 15.—M. H., a man, aged 49, the onset of whose illness was at the age of 48, was admitted to the Psychiatrische Klinik, Munich, on March 23, 1925, and treated with malaria. He had a short remission but was readmitted on May 16, 1926, and died on May 17. He had several petit mal attacks between January and May, 1925. No record of the necropsy observations was available. Microscopically, the brain showed the changes of dementia paralytica and sclerosis of the cornu ammonis.

CASE 16.—A. S., a man, aged 45, the onset of whose illness was at the age of 36, was admitted to the Psychiatrische Klinik, Munich, on Aug. 28, 1927, and died forty-eight hours later. The patient had had an apoplectiform attack eight days before admission, but there was no mention of epileptiform attacks. No history of any therapy or record of the necropsy observations was available. Microscopically, the brain showed the changes of dementia paralytica with sclerosis of the cornu ammonis.

CASE 17.—O. B., a woman, aged 31, the onset of whose illness was at the age of 26, was admitted to the Psychiatrische Klinik, Munich, on March 16, 1914, and was treated with arsphenamine. She was released in June, 1914, and had a remission until April, 1918, when she was again admitted to the Psychiatrische Klinik, and she was transferred to the Heil und Pflegeanstalt, Haar, on May 8, 1918. The patient first had epileptic convulsions on July 26, 1918, and these continued intermittently until death in status epilepticus on Aug. 1, 1919. No record of the necropsy observations was available. Microscopically, the brain showed the changes of dementia paralytica and sclerosis of the cornu ammonis.

CASE 18.—No record was available in this case, except that the brain was that of S., a woman in the early thirties, who died after a short illness characterized by convulsions and progressive dementia. The brain was brought to Dr. Spielmeyer for histologic examination. Microscopically, it showed signs typical of dementia paralytica and sclerosis of the cornu ammonis on both sides.

CASE 19.—H. S., a man, aged 20, the onset of whose illness was at the age of 16, was admitted to the Psychiatrische Klinik, Munich, on Aug. 27, 1920, having previously been in the Irrenanstalt at Dösen. He was transferred to the Heil und Pflegeanstalt, Eglfing, on Sept. 13, 1920. The patient had numerous convulsions in the period between May 4, 1922, and November 28. No mention of epileptic convulsions was made from this date until death on Aug. 19, 1923, of pulmonary tuberculosis. Necropsy showed tuberculosis of the lungs. Microscopically, the brain showed signs typical of dementia paralytica and sclerosis of the cornu ammonis.

CASE 20.—U. S., a man, aged 51, was admitted to the Psychiatrische Klinik, Munich, on May 17, 1924, in a demented state. No history was obtainable. For several days before death he had epileptic convulsions, and he died on May 17, 1924, in status epilepticus. No record of the necropsy was available. Microscopically, the brain showed signs typical of dementia paralytica and sclerosis of the cornu ammonis.

CASE 21.—M. W., a man, aged 42, the onset of whose illness was at the age of 39, was admitted to the Psychiatrische Klinik, Munich, on Oct. 2, 1924, and given malarial therapy. He was released on Dec. 12, 1924, and had a partial remission until Feb. 1, 1927, when he was readmitted on account of attacks that were not further described. He was released on March 18, 1927, and readmitted on July 4, in an unconscious state following an epileptic convulsion. He had another spell of unconsciousness (not further described in the history) on July 29, 1930, in which he died. Necropsy showed syphilitic aortitis, bronchopneumonia, infarcts in the kidneys and chronic cystitis. Microscopically, the brain showed the usual signs of dementia paralytica and sclerosis of the cornu ammonis.

CASE 22.—J. F., a woman, aged 35, the onset of whose illness was at the age of 31, was admitted to the Psychiatrische Klinik, Munich, on April 3, 1925, and transferred to the Heil und Pflegeanstalt, Haar, on April 23. In March, 1926, the patient had many convulsions, and remained in status epilepticus for several days

during the month. She died on Feb. 7, 1927; marasmus and sepsis were given as the causes of death. No record of treatment or necropsy observations was available. Microscopically, the brain showed the usual changes of dementia paralytica, sclerosis of the cornu ammonis and numerous small metastatic abscesses scattered throughout the brain; in addition, two small "Erweichungsherde" were present in the white matter of the parietal lobe.

Case 23.—L. L., a man, aged 36, the onset of whose illness was at the age of 30, was admitted to the Psychiatrische Klinik, Munich, on Jan. 19, 1925, and treated with arsphenamine and by inoculation with recurrent fever. He was released on April 20, 1925, and had a partial remission until Oct. 30, 1926. In the interval he had one epileptic convulsion. He was inoculated with malarial fever and released on June 23, 1927. Following another partial remission he was readmitted to the Klinik on April 17, 1928, and transferred to the Heil und Pflegeanstalt, Eglfing, on June 11. Convulsions were noted daily (from six to eight) in the period between Jan. 20 and Jan. 25, 1930, and the patient died in status epilepticus on April 19. Necropsy showed actinomycosis of the lungs, polycystic kidneys and macroscopic evidence of dementia paralytica in the brain. Microscopically, the brain showed signs typical of dementia paralytica and sclerosis of the cornu ammonis.

Case 24.—F. T., a man, aged 46, the onset of whose illness was at the age of 33, while in the army, in 1916, was admitted to the hospitals on numerous occasions on account of mental disturbances. After discharge from the army he was treated in various hospitals for mental diseases until admission to the Heil und Pflegeanstalt, Haar, on April 14, 1924, where he remained until death on Jan. 18, 1930. He had received sporadic treatment since the initial infection in 1905, consisting of mercury, arsenic and bismuth. The patient had two fainting spells in 1916, at the time of the onset of the illness, and numerous epileptic convulsions between May 12, 1928, and Jan. 18, 1930, when he died in status epilepticus. No report of the necropsy observations was available. The brain showed the lesions typical of dementia paralytica, with status spongiosus in the right temporal and occipital lobes and sclerosis of the cornu ammonis on the right side.

Case 25.—F. W., a man, aged 54, the onset of whose illness was at the age of 53, was admitted to the Psychiatrische Klinik, Munich, on June 9, 1925, and treated by inoculation with recurrent fever. He was released on Sept. 3, 1925, but was readmitted on Dec. 6, 1925, and transferred to the Heil und Pflegeanstalt, Haar, on Jan. 4, 1926, where he died on January 26. No mention of convulsions was found in the records. Necropsy showed marasmus, atrophy of the internal organs, chronic tuberculosis of the lungs and macroscopic signs of dementia paralytica in the brain. Microscopically, the brain showed signs typical of dementia paralytica and fresh ischemic changes in Sommer's sector of the cornu ammonis.

Case 26.—W. T., a man, aged 63, the onset of whose illness was at the age of 61, was admitted to the Psychiatrische Klinik, Munich, on Feb. 4, 1927, and treated with arsphenamine and mercury. He was transferred to the Heil und Pflegeanstalt, Eglfing, on April 14, 1927, and died on April 28. No mention of convulsions was found in the records. Necropsy showed syphilitic aortitis, bronchopneumonia, pyelitis and macroscopic signs of dementia paralytica in the brain. Microscopically, the brain showed signs of typical dementia paralytica and sclerosis of both cornua ammonis.

Case 27.—M. M., a woman, aged 48, was brought to the Psychiatrische Klinik, Munich, on July 2, 1930, by the police; no clinical history was obtainable. On neurologic examination a diagnosis of dementia paralytica was made. She was

treated by inoculation with malarial organisms. She had a generalized convulsion three days before death on Oct. 19, 1930. Examination of the brain showed macroscopically and microscopically the picture typical of Lissauer's dementia paralytica and sclerosis of the cornu ammonis on the right side.

CASE 28.—J. S., a man, aged 23, the onset of whose illness was at the age of 12, was brought to the Psychiatrische Klinik, Munich, on June 16, 1926. He was inoculated with malarial organisms, after which he had a partial remission for about a year. He was readmitted on June 31, 1927. He had numerous generalized and jacksonian epileptic convulsions in the last one and one-half years of life, and also a left hemiplegia. He died on Nov. 16, 1928. Macroscopically and microscopically, the brain showed the changes typical of Lissauer's dementia paralytica with sclerosis of the cornu ammonis on the right side.

CASE 29.—M. I., a woman, aged 60, the onset of whose illness was at the age of 54, was admitted to the Psychiatrische Klinik, Munich, on Nov. 18, 1924. She was treated with arsphenamine and mercury. For the six years before admission, the patient had had attacks of transient amblyopia, and during the last year of life she had convulsive attacks confined to the right half of the body and an aphasic speech disturbance. She died on May 26, 1927, of facial erysipelas. The brain showed the signs typical of Lissauer's dementia paralytica with sclerosis of the cornu ammonis on the left side.

CASE 30.—W. K., a man, aged 54, the onset of whose illness was at the age of 41, was admitted to the Psychiatrische Klinik, Munich, on Aug. 27, 1918. He was released on Dec. 8, 1918, and was not readmitted until Sept. 29, 1922. He was transferred to the Heil und Pflegeanstalt, Gabersee, on Oct. 22, 1922, where he remained until death on Jan. 31, 1931, of bronchopneumonia. In 1928 and 1929, he had numerous generalized and jacksonian epileptic attacks which were followed by a left hemiplegia. Necropsy showed bronchopneumonia, syphilitic aortitis, verrucose endocarditis of the aortic valve, pyelitis and pyelonephritis. The brain showed the changes typical of Lissauer's dementia paralytica with sclerosis of the cornu ammonis on the right side.

RÉSUMÉ OF THE LITERATURE ON SCLEROSIS OF THE CORNU AMMONIS IN DEMENTIA PARALYTICA

Little has appeared in the literature on the relationship of sclerosis of the cornu ammonis in dementia paralytica to the epileptic convulsions occurring in this disease. Sclerosis of the cornu ammonis in dementia paralytica has been reported by Spielmeyer,[5] Uchimura,[5] Taft,[8] Pfleger,[8] Bodechtel,[23] Bratz,[8] Alzheimer[8] and Borosdin.[8] Jelliffe and White[8] gave an illustration in their textbook of such a lesion, and stated that clinically the case had shown convulsions.

Pfleger[8] was the first to mention the occurrence of sclerosis of the cornu ammonis in dementia paralytica in 1880. He concluded that this condition was due to a nutritional loss caused by alterations in the circulation during and following convulsions. Bratz,[8] in 1899, reported several cases of sclerosis of the cornu ammonis in patients with dementia paralytica, and he stated that it was present in 20 per cent of such cases and was found in cases characterized clinically by numerous

convulsions. He suggested that a tentative diagnosis of sclerosis of the cornu ammonis could be made during life in such cases. In later articles, however, he claimed that there was no relation between the sclerosis of the cornu ammonis and convulsions during life. His article published in 1923 [8] with regard to sclerosis of the cornu ammonis in epilepsy and dementia paralytica is difficult to understand. He reported twenty-nine cases of dementia paralytica, twelve of which showed sclerosis of the cornu ammonis, in none of which were there convulsions (Krämpfe). He said further, however, that in confirmation of Spielmeyer's statement the cell loss in Sommer's sector was found in all cases with acute exacerbations, "status epilepticus" or "paralytische Anfälle ohne Krämpfe." It is not clear whether he is speaking of essential epilepsy or of dementia paralytica, but it is probably the latter. It is difficult to believe that in an unselected group of cases as large as this there were no cases with convulsions, as Kraepelin [24] observed them in 30 per cent of cases of dementia paralytica in the Heidelberg clinic and in 60 per cent of cases in his clinic at Munich.

Taft,[6] in 1920, reported her observations on nineteen cases of dementia paralytica with convulsions, and in all of her cases except one there was sclerosis of the cornu ammonis.

COMMENT ON CASES

From a review of the thirty cases (summarized in the accompanying table), it can be seen that twenty-six showed typical convulsive attacks; one case (case 11) showed petit mal attacks, one (case 16) showed an apoplectiform attack, and in two cases (cases 25 and 26) no record of such attacks was found. It is possible that in the two latter such attacks may have occurred and were not recorded in the anamnesis; such an hypothesis, however, will not be considered seriously, as Spielmeyer has shown that functional disturbances in the cerebral circulation can occur and occasion cerebral lesions without the appearance of convulsive phenomena. He has found such lesions in cases of hypertension and various intoxications without demonstrable changes in the blood vessels, and he has also found a sclerosis of the cornu ammonis in the brain of a patient with dementia paralytica who had had no convulsive seizures during life. Bratz also has reported such cases as have been mentioned.

No attempt was made to determine the age of the sclerotic lesion in the cornu ammonis. It seems significant, however, that in cases 4 and 9, in which the convulsions first appeared one and nine days, respectively, before the death of the patients in status epilepticus, the change in the

24. Kraepelin and Lange: Psychiatrie, Leipzig, Johann Ambrosius Barth, 1927.

cells of Sommer's sector and the end-plate of the cornu ammonis was that of the severe ischemic variety described by Spielmeyer.[18] Cases 11 and 13, in which the convulsions first appeared a few days before death, showed a slightly advanced stage of degeneration in the cornu ammonis. Many of the ischemically changed cells had apparently dropped out; others stained very faintly with the Nissl stain, and the glial reaction was much more marked.

Summary of Thirty Cases of Dementia Paralytica with Sclerosis of the Cornu Ammonis, Showing the Relative Incidence of Convulsions

Case	Age	Sex	Duration of Disease, Years	Convulsions		Comment
				Frequency	Duration	
1. A. B.	43	M	8	++++	7 years	
2. E. B.	55	F	5	++++	1 month	Died in status
3. K. G.	50	M	1	++++	1 year	Died in status
4. K. L.	46	M	4	+	1 day	Died in status
5. B. W.	40	F	3	+++	8 months	
6. M. P.	51	M	4	++++	4 years	
7. E. M.	16	M	6	+++	1 year	
8. T. G.	33	F	4	++++	4 years	
9. A. S.	19	F	3	++	9 days	Died in status
10. O. Z.	30	M	5	++++	5 years	
11. J. T.	22	M	9	++++	7 years	Died in status
12. J. S.	53	M	1	++	18 days	Died in status
13. L. W.	39	M	10	+	3 days	Died in status
14. R. H.	43	M	1	++	9 months	
15. M. H.	49	M	1	++*	5 months	
16. A. S.	45	M	9	0		
17. O. B.	31	F	5	+++	1 year	Died in status
18. S.	..	F	..	+		
19. H. S.	20	M	4	++++	1 year	
20. U. S.	51	M	..	+	.....	Died in status
21. M. W.	42	M	3	+	7 days	Died in status
22. J. F.	35	F	4	+++	1 year	
23. L. L.	36	M	5	+++	1 year	Died in status
24. F. T.	46	M	13	++++	2 years	Died in status
25. F. W.	54	M	1	0	0	
26. W. T.	63	M	2	0	0	
27. M. M.	48	F	..	+	1 day	
28. J. S.	23	M	11	++++	1½ years	
29. M. I.	60	F	6	+++	1 year	
30. W. K.	54	M	13	+++	2 years	

* The patient had petit mal attacks.

Five were cases of juvenile dementia paralytica and six cases (7, 24 and 27 to 30) were of the so-called Lissauer type, and will be more fully described in a later publication. The average duration of the disease was 6.6 years for the juvenile group, and 5.1 years for the twenty-two adult cases in which it was possible to determine the duration of the disease. This is somewhat longer than that given by Kraepelin,[24] but it is in agreement with his statement that the duration of the disease is longer in cases with convulsions than in those without convulsions. In many of the cases the convulsions occurred only a few months or days

before death; in others (cases 1, 6, 8, 10 and 11), the convulsions occurred at intervals for more than four years before death. Twelve of the patients died in status epilepticus.

The ages of the patients with convulsions varied between 16 and 60 years. In none of the cases were any noteworthy arteriosclerotic changes found in the cerebral blood vessels. Cases 3 and 22, both of patients dying of marasmus and sepsis, showed embolic lesions in other parts of the brain. Emboli were not found in the vessels of the cornu ammonis in these two cases, but as serial sections were not made the possibility of such lesions cannot be excluded.

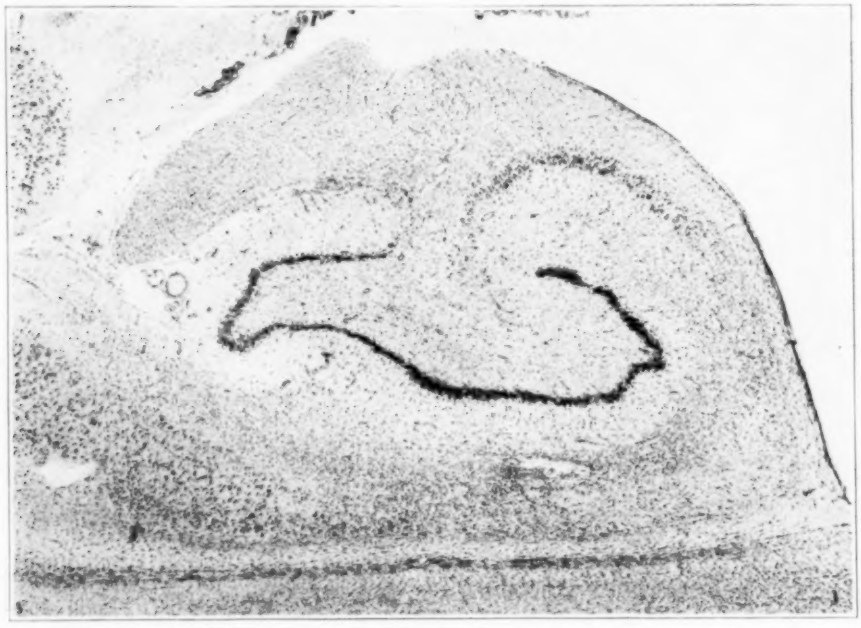

Fig. 1 (case 23).—Section from the cornu ammonis, showing a relatively fresh sclerosis in the presence of a very mild degree of perivascular infiltration. Numerous convulsions were noted in this case during the last four months of life. Nissl stain; × 13.

An attempt was made to correlate the severity of the changes in the cornu ammonis with the grade of inflammatory reaction around the blood vessels in order to ascertain if these changes could be due to the vascular disturbances accompanying this inflammation, but no such relationship was found. In many of the cases here reported there was only a very slight degree of inflammatory reaction around the vessels, and in others the perivascular infiltration was striking. It could possibly be assumed that in the cases with an old sclerotic lesion, in which the inflammatory changes were mild, this reaction had been formerly present and

had disappeared; this assumption could not be made, however, in several cases in which the changes in the cornu ammonis were fresh (ischemic) and the inflammatory reaction mild, as in cases 4 and 8; in several other cases with mild inflammatory changes, the sclerosis of the cornu ammonis was evidently of recent origin. In many of the cases evidence of fresh changes could be found superimposed on undoubtedly older lesions, which indicates a repetition of the injurious process. On the other hand, a marked infiltration of the meninges and cortical vessels of this region is often found in dementia paralytica without sclerosis of the cornu

Fig. 2 (case 10).—Section from the cornu ammonis, showing a complete loss of cells in Sommer's sector and in the end-plate. The perivascular infiltration is just as marked in the well preserved subiculum as in the sclerotic Sommer's sector. Numerous convulsions were noted in this case during the five years of the patient's illness. Nissl stain; × 13.

ammonis, or any more marked degenerative changes than are found elsewhere in the brain. It would therefore seem that the fresh ischemic changes in the ganglion cells and the sclerotic lesion of the cornu ammonis in dementia paralytica are not caused by a circulatory disturbance dependent on the inflammatory reaction for its origin. Figure 1 shows a typical sclerosis accompanied by a very slight degree of perivascular infiltration, and as a contrast figure 2 shows the same lesion accompanied by a very marked degree of vascular inflammatory reaction.

These sections were from cases (cases 23 and 10) characterized clinically by numerous convulsions. Figure 3, from case 26, illustrates that the lesion can be found also in patients who have not had convulsive attacks, as was previously stated.

With no evidence of an organic occlusion of the vessels in the cornu ammonis in these cases, the changes must be considered as due to a functional disturbance of the circulation, and the presence of epileptiform phenomena in 90 per cent of the cases strongly indicates a causal relationship between this disturbance of the circulation and the epileptic

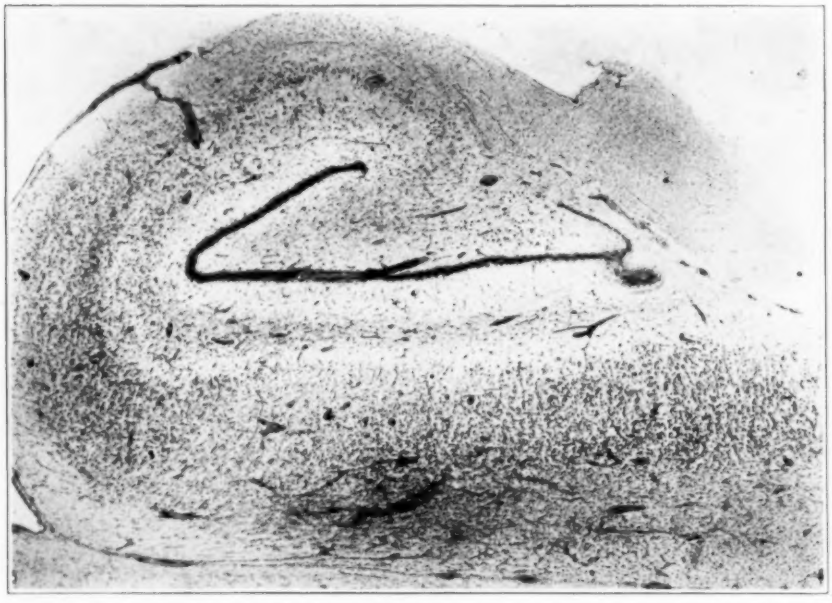

Fig. 3 (case 26).—Section from the cornu ammonis, showing a picture similar to that in figure 2. No convulsions were noted in this case. Nissl stain; × 13

convulsions. It is undoubtedly true that functional disturbances of the circulation occur in other portions of the brain and occasion lesions there, and the fact that evidence of such vascular disturbances is more often found in the cornu ammonis is probably due to the greater vulnerability of this region. Lesions of other parts of the brain on the basis of a functional vascular disturbance have been reported in various conditions by Neubürger,[1] de Vries,[1] Bodechtel,[9] von Braunmühl,[14] Benoit [25] and others. Such lesions also occur in dementia paralytica, as will be shown in a later study.

25. Benoit, W.: Ein Beitrag zur Kenntnis der Rindenveränderungen bei Wochenbettseklampsie, Ztschr. f. d. ges. Neurol. u. Psychiat. **131**:602, 1931.

SUMMARY

1. Evidence is presented showing that sclerosis of the cornu ammonis is of vascular origin.

2. Thirty cases of dementia paralytica with sclerosis of the cornu ammonis are reported; the incidence of epileptiform phenomena was found to be 90 per cent.

3. No evidence of an organic vascular occlusion was found in these cases, and there was no apparent causal relation between the sclerosis and the inflammatory reaction around blood vessels.

CONCLUSIONS

Functional disturbances of the circulation (vascular spasms) occur in dementia paralytica as shown by the lesion in the cornu ammonis. The coincidence of epileptiform phenomena in such a large percentage of these cases must indicate a causal relationship between the vascular spasm and the epileptiform phenomena. The exact relationship of this vascular spasm to the convulsion is not known. As claimed by Spielmeyer, the vascular spasm is only one link in the chain of events in the convulsive seizure, but at present ischemia is the only link that can be demonstrated histologically.

THE DISTRIBUTION OF CALCIUM BETWEEN BLOOD AND CEREBROSPINAL FLUID IN SLEEP INDUCED BY DIALLYL-BARBITURIC ACID

AN EXPERIMENTAL STUDY *

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This study has been suggested by the results obtained in a previous investigation of the behavior of calcium in blood during sleep induced by diallyl-barbituric acid.[1] The question has arisen whether the diminution of the calcium content in blood observed in most experiments performed during sleep was accompanied by any corresponding modifications of the calcium content of the cerebrospinal fluid. Moreover, it appeared worth while to compare the measurements of the fluid calcium with those of the blood calcium; that is, to study the fluid calcium-blood calcium ratios in the light of the following concepts: (1) the idea of Cloetta and Thomann,[2] according to which the diminution of calcium in blood during sleep is associated with a shift of calcium from the blood to the brain; (2) the dominant view on the function of the hemato-encephalic barrier and the rôle of the cerebrospinal fluid; that is, that the latter is the intermediary body in the process of exchange between the general circulation and the nervous system.[3] Thus, the level of the permeability of the barrier to calcium during sleep, as determined by the fluid calcium-blood calcium ratio, may be of significance in the discussion of Cloetta's and Thomann's concept. However, the hypothesis of these authors has been subjected to a test made in a more direct way, namely, an experimental study of the calcium content of the whole brain and various parts of the brain during sleep. The results of this study will be recorded in another communication.

METHOD OF INVESTIGATION

The study was carried out on cats. Deep sleep was induced by diallyl-barbituric acid (dial ciba) given intramuscularly in doses of from 1.5 to 2 cc.

* Submitted for publication, June 2, 1931.

* From the Henry Phipps Psychiatric Clinic, Department of Internal Medicine, Johns Hopkins Hospital.

1. Katzenelbogen, S.: The Blood Electrolyte Changes in Narcosis, with Special Reference to Calcium and Potassium: An Experimental Study, Arch. Neurol. & Psychiat. **24**:525 (Sept.) 1930.

2. Cloetta and Thomann: Chemisch-physikalische Untersuchungen zur Theorie der Narkose, Arch. f. exper. Path. u. Pharmakol. **103**:260, 1924.

3. Katzenelbogen, S.: The Physiopathological Significance of the Meningeal Permeability, Am. J. Psychiat. **10**:235, 1930.

After from eighteen to twenty-two hours of sleep and while the animals were still asleep, samples of blood and cerebrospinal fluid were obtained. Blood was secured by heart puncture and fluid by cisternal puncture. The experimental studies made on twenty animals during sleep were duplicated by twenty control experiments. In the control animals, blood and fluid were withdrawn twice, at the beginning of the experiments and then between eighteen and twenty-two hours later, as in the studies on the animals during sleep, while the animals were in the waking state. The experiments made on animals in which sleep had been induced and those made on controls were carried out under similar conditions. All animals were kept without food in the intervals between the two withdrawals of blood and fluid.

Analysis of Calcium.—In both the blood and the cerebrospinal fluid, calcium was determined by the method of Trevan and Bainbridge.[4] This method presents the advantage of giving adequate results even with material containing small quantities of calcium. It proved, therefore, to be particularly useful in this study, as only small amounts of cerebrospinal fluid were available; 1 cc. of blood serum and fluid, respectively, was used. In order to check the method, analyses were carried out with 1 cc. and 0.5 cc. of a calcium solution containing 10.5 mg. per hundred cubic centimeters; they showed that the error of the method may be within the absolute amount of ± 0.005 mg. This error corresponds to approximately ± 5 per cent in the analysis of blood serum and ± 10 per cent in the analysis of cerebrospinal fluid when 1 cc. of each is used, as has been the procedure employed. Only variations of greater magnitude than the technical errors mentioned will be considered.

CALCIUM IN THE BLOOD AND THE CEREBROSPINAL FLUID, AND FLUID CALCIUM-BLOOD CALCIUM RATIOS DURING SLEEP

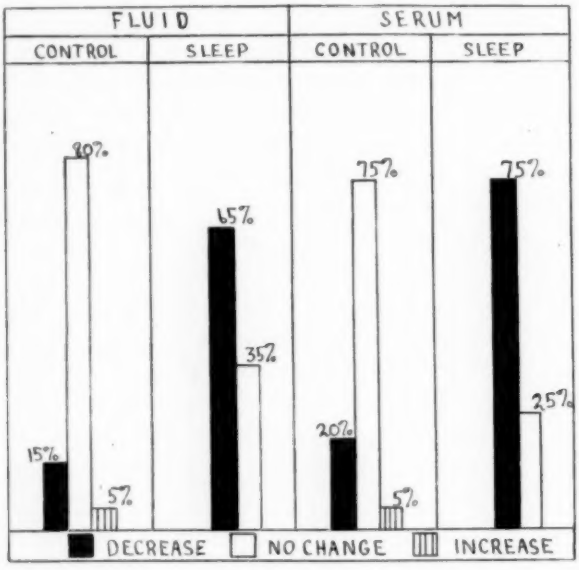
The twenty experimental studies were performed on twenty cats during sleep. The serum calcium of blood, withdrawn before diallyl-barbituric acid was given, ranged between 8.4 and 10.7 mg. per hundred cubic centimeters of blood. During sleep, the range of the serum calcium was within 6.5 and 10.2 mg. per hundred cubic centimeters. A comparative study of the figures obtained in the twenty experimental studies made on animals during induced sleep and in the waking state shows that the blood calcium underwent the following modifications during sleep: In fifteen (75 per cent) of the twenty sleeping cats, a decrease in the serum calcium content was found, and in five (25 per cent) no change was found.

In each of the experiments the cerebrospinal fluid was withdrawn at the same time as the blood. The calcium content of the specimens obtained before the hypnotic was given ranged from 4.1 to 6.6 mg. per hundred cubic centimeters. In the samples of cerebrospinal fluid withdrawn during sleep, the calcium content ranged between 3.5 and 5 mg. per hundred cubic centimeters. The fluid calcium during sleep,

4. Trevan, J. W., and Bainbridge, H. W.: Estimation of Calcium in Blood Serum, Biochem. J. **20**:423, 1926.

as compared in each experiment with the corresponding fluid calcium during the waking state, shows a decrease during sleep in thirteen of the twenty animals (65 per cent) and no change in seven (35 per cent). In none of the experiments did calcium increase either in the blood or in the cerebrospinal fluid during sleep.

As to the ratio of fluid calcium to blood calcium, my observations may be summarized as follows: In the waking state, that is, before the hypnotic was given, the fluid calcium-blood calcium ratios ranged within from 0.43 to 0.61. During sleep, the ratios were from 0.37 to 0.62. In three (15 per cent) of the twenty animals, the ratios were lower



Changes in the calcium content of the blood and the cerebrospinal fluid during sleep.

during sleep, and in one case (5 per cent), higher as compared with the corresponding ratios of the waking state. In sixteen cats, the fluid calcium-blood calcium ratios ranged within the same limits during sleep as during the waking state.

CONTROL EXPERIMENTS

The control study was carried out, as already mentioned, on twenty cats. In each, two specimens of blood were obtained at intervals of from eighteen to twenty-two hours. The serum calcium determinations gave the following results: In the twenty samples of blood from the first punctures, the calcium ranged between 8.8 and 10.5 mg. per hun-

dred cubic centimeters. In the second twenty specimens, calcium was found to be within the limits of 8.5 and 10.5 mg. per hundred cubic centimeters. A spontaneous diminution in the calcium content had taken place in four cats (20 per cent), an increase in one cat (5 per cent) and no changes, beyond the limits of technical errors, in fifteen cats (75 per cent).

The cerebrospinal fluid was obtained in each cat immediately after the heart puncture. In twenty specimens from the first cisternal puncture, the fluid calcium ranged from 4.5 to 6.2 mg. per hundred cubic centimeters. In the twenty samples obtained from the second punctures, the fluid calcium was within from 4.3 to 6.5 mg. per hundred cubic centimeters. The spontaneous changes in the calcium content in the second specimens consisted of: a decrease in three cases (15 per cent). an increase in one case (5 per cent) and no changes in sixteen cases (80 per cent).

The fluid calcium-blood calcium ratios derived from the respective figures for calcium in the specimens of blood and fluid from the first heart and cisternal punctures ranged within 0.46 and 0.66. The ratios obtained from the second punctures were found to be between 0.45 and 0.60. Among the last named ratios, two are slightly below the corresponding ratios obtained from the first punctures. In eighteen (90 per cent) of the twenty experiments, no change had taken place.

COMMENT

A comparative study of the results obtained in the twenty cats during sleep with those of the observations made on the twenty control animals, as shown in the accompanying chart, leads to the following statements: A decrease of calcium in the blood proves to be characteristic of hypnotic sleep, as shown by the discovery of a marked decrease in 75 per cent of the animals when sleep was induced against 20 per cent of the controls in which a spontaneous chance diminution was found. These data corroborate the previous observations on the behavior of blood calcium during hypnotic sleep.[1] The fluid calcium follows the trend of blood calcium. It is shown to be diminished in 65 per cent and not to change in 35 per cent of the cats during sleep, as compared with a spontaneous decrease in 15 per cent, an increase in 5 per cent and no changes in 80 per cent of the control animals. Thus, a low fluid calcium was found during sleep in a smaller percentage of animals than a low blood calcium; i. e., the fluid calcium was low in 65 per cent and the blood calcium in 75 per cent. This discrepancy may suggest that in 10 per cent of the animals in the sleeping state, the fluid calcium was relatively increased, as it did not follow the decrease of calcium in the blood. On the other hand, the fluid calcium-blood calcium ratios show that in some cases calcium displays a tendency

toward a proportionately greater decrease in the fluid than in the blood. This may be seen in the observation that in three (15 per cent) of the twenty cats in the sleeping state experiments, the ratios were lower during sleep than before the hypnotic was given. It is obvious that if the decrease of calcium in the fluid were proportional to the decrease in the blood, the ratios would not change. It should be emphasized, however, that a spontaneous diminution of the ratio was also observed in two of the control animals.

SUMMARY AND CONCLUSIONS

1. The calcium content of the blood and that of the cerebrospinal fluid and the fluid calcium-blood calcium ratios were investigated in twenty cats during sleep induced by diallyl-barbituric acid.

2. In each cat, blood was withdrawn by heart puncture, and the cerebrospinal fluid by cisternal puncture before the hypnotic was given and again, from eighteen to twenty-two hours later, while the animals were still in deep sleep.

3. A control study was carried out on twenty cats (twelve of which were also used for the experiments during induced sleep) in which blood and fluid were withdrawn twice, before the experiments and after an interval of from eighteen to twenty-two hours.

4. The blood calcium decreased in 75 per cent of the twenty cats during sleep, as compared to a spontaneous decrease in 20 per cent of the twenty control animals which were awake.

5. The fluid calcium showed a diminution in 65 per cent of the twenty sleeping animals, as compared with a spontaneous diminution in 15 per cent of the twenty control animals.

6. In three of the twenty experiments on sleeping animals, the fluid calcium-blood calcium ratios were found lower during sleep than in the waking state; a spontaneous decrease of the ratios occurred in two of the twenty control animals.

7. Both the blood calcium and the cerebrospinal fluid calcium tend to decrease in hypnotic sleep in most cases.

8. The fluid calcium-blood calcium ratios do not suggest that sleep would be associated with marked changes in the permeability to calcium of the barrier between the blood and the cerebrospinal fluid.

EPHEDRINE CIRCULATORY AND GLYCEMIC REACTIONS IN THE PSYCHOSES*

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There have been numerous investigations of the neurovegetative states accompanying affective reactions. It has been demonstrated that the affective disorders are accompanied by measurable alterations in the sympathetic tonus; the manic-depressive psychoses show reactions indicative of sympathetic hypertonus and the schizophrenias give responses indicating states varying from obtundity of the sympathetic to frank vagotonia. Claude and his co-workers [1] found this neurovegetative loss of balance to be a most striking feature of the psychoses. They stated that pharmacologic tests and visceral reflexes elicit responses of an intensity found only in psychotic patients. The existence of a demonstrable vagotonia in the schizophrenias has been questioned by some authorities, who prefer to think of the catatonic and hebephrenic types as showing merely atony of the neurovegetative system as a whole. Cannon [2] has shown that vegetative disturbances attend affective experiences, and, if often enough repeated, these affective experiences may condition the responses of the sympathetic portion of the vegetative nervous system. He believed that affective experiences sensitize the sympathetic to the degree that even mild stimuli produce extreme reactions.

This affective conditioning of visceral responses has been the basis for most objective psychiatric diagnostic procedures. Chief use has been made of the pharmacodynamic tests employing atropine, pilocarpine or epinephrine as a means of demonstrating the relative hypertonicity or hypotonicity of one or the other division of the vegetative system. Considerable vagueness engulfs the workings of the sympathetic and vagus systems in the psychoses. It is not the purpose of this

* Submitted for publication, March 2, 1931.

* Read at the Eleventh Annual Meeting of the Association for Research in Nervous and Mental Disease, New York, Dec. 30, 1930.

* From the Laboratories of the Institute and Department for Mental and Nervous Diseases, Pennsylvania Hospital.

1. Claude, H.; Santenoise, D., and Targowla, R.: An Attempt at Biologic Diagnosis of States of Excitement and Depression, Arch. Neurol. & Psychiat. **13**:729 (June) 1925.

2. Cannon, W. B.: Bodily Changes in Pain, Hunger, Fear and Rage, New York, D. Appleton and Company, 1929.

paper to clarify the psychiatric aspects of the problem, but simply to record our observations in a number of well established psychotic reactions and to call attention to the consistent responses of the manic-depressive psychoses as a group as contrasted with the schizophrenias. The schizophrenias here considered include the hebephrenic, catatonic and simple types, or those which are sometimes classified as the affect-less reactions. It appears in our series of cases that the affective group reacts in a manner consistently different from the schizophrenic in a series of cardiovascular and glycemic responses to identical pharmacologic stimuli.

Ephedrine hydrochloride was employed in our tests since its sympathicomimetic action seems well established. Chen and Schmidt,[3] in a recent monograph, have expressed this view and the observation is supported by abundant research. There are some investigators, however, who assert that the drug acts by direct stimulation of smooth muscle. All writers are in agreement, nevertheless, as to the epinephrine-like action of the drug. Ephedrine has several distinct advantages over epinephrine. The blood pressure rise in response to the drug is more enduring, lasting from seven to ten times longer than that from epinephrine; it can be used in from ten to one hundred times the strength of epinephrine; its effect is less intense and the reaction of the patient less stormy in nature. Ephedrine is said to produce the same circulatory and glycemic actions as epinephrine, namely, a rapid rise in blood pressure and an increase in blood sugar. The glycemic response to ephedrine has been reviewed by Chen and Schmidt. Recently, Rodoslav and Stoicescu[4] studied the effect of intravenous ephedrine in normal men. They employed doses of from 5 to 90 mg. and obtained consistent results. A diphasic curve was observed in the blood sugar variations, a primary hyperglycemia followed by a hypoglycemia with a return to the normal fasting level in two hours.

LITERATURE

In recent years, many efforts have been made to make objective tests an essential part of the psychiatric diagnostic armamentarium. Kirby,[5] in 1921, in an outline dealing with the methods of psychiatric clinical examinations, listed three pharmacologic tests making use of

3. Chen, K. K., and Schmidt, C. F.: Ephedrine and Related Substances, Medicine **9**:1 (Feb.) 1930.

4. Rodoslav, C., and Stoicescu, C.: Wirkung intravenös einverleibter abgestufter Ephedrinlosungen auf den Blutzucker und Blutdruck beim Menschen in Verleich mit Adrenalin, Wien. klin. Wchnschr. **41**:1775, 1928.

5. Kirby, G. H.: Guides for History Taking and Clinical Examination of Psychiatric Cases, Utica, N. Y., State Hospital Press, 1921.

pilocarpine, atropine or epinephrine. These methods have the same basic theory—the measurement of the responses of the vegetative nervous system to the drug. These observations are taken as an index to the tonus or degree of excitability of one or the other division of the vegetative nervous system.

Blood sugar values in the psychoses have been studied by Smith and Hill,[6] who found the blood sugar curve generally low in cases of dementia praecox and demonstrated that thyroid extract had the effect of heightening the curves. Mumford and Parkin[7] studied the blood sugar fluctuations in the emotional states and found the highest increase during affective disorders. They stated that the blood sugar values were increased in proportion to the degree of affective disturbance. Other investigations of the sugar metabolism in the psychoses have been carried out. Lorenz[8] and others have found sugar tolerance in manic-depressive psychoses higher than in other disorders. Research in our laboratories under the direction of Dr. C. B. Farr has confirmed this observation of abnormally heightened sugar tolerance in the affective psychoses.

Gordon, Ostrander and Counsell[9] studied the epinephrine glycemic curves in a group of seven schizophrenic patients and a number of normal and psychotic controls. They concluded that the manic-depressive patients showed a different type of rise and fall, and asserted that the test was of diagnostic significance. Raphael and Parsons[10] tested the glycemic responses of a number of mentally ill patients to intramuscular injections of epinephrine and found a rise reaching a maximum at thirty minutes to one hour in cases classed as dementia praecox, while the other types showed variable curves. Mann[11] has shown that abnormal blood sugar curves in some psychotic patients return to normal when the patients recover from the psychoses, and that bringing abnormal blood sugar curves closer to normal (by glandular therapy) is coincident with improvement. Mann believed that any attempt to investigate the individual's sensitiveness to epinephrine stimulation as

6. Smith, J. F., and Hill, H. G.: The Blood Sugar Curve in Dementia Praecox, J. Ment. Sc. **73**:265, 1927.

7. Mumford, P. B., and Parkin, G. G.: Some Observations of the Fasting Blood Sugar in Certain Mental States, J. Ment. Sc. **69**:330, 1923.

8. Lorenz, W. F.: Sugar Tolerance in Dementia Praecox and Other Mental Disorders, Arch. Neurol. & Psychiat. **8**:184 (Aug.) 1922.

9. Gordon, H.; Ostrander, J., and Counsell, S.: The Adrenalin Glycemic Curve as a Diagnostic Aid in Psychiatry, Am. J. Psychiat. **7**:183, 1927.

10. Raphael, T., and Parsons, J. P.: Metabolism Studies in Dementia Praecox and Manic-Depressive Insanity: Glycemic Reactions to the Intramuscular Administration of Epinephrine, Arch. Neurol. & Psychiat. **8**:172 (Aug.) 1922.

11. Mann, S. A.: Blood Sugar Studies in Mental Disorders, J. Ment. Sc. **71**: 443, 1925.

indicated by the blood sugar response must be made by determining the dose necessary to produce a given response rather than the effect produced by a given dose.

The mechanism of this variation of the glycemic curves in the psychoses is not clear. Several investigations have been made of sugar mobilization from the liver in normal states and in hepatic disease. Brill [12] has shown that epinephrine glycemic curves are of value in demonstrating severe parenchymatous hepatic destruction, and in a series of patients with hepatic disease he was able to demonstrate a retarded sugar mobilization. This delayed glycogenolysis has been proved to be of purely hepatic origin by the work of Kotschneff.[13] She has shown that the increase of blood sugar following the injection of epinephrine is exclusively conditioned by the mobilization of glycogen from the liver. Kugelmann [14] has likewise investigated parenchymatous liver disease by this technic and has computed a hyperglycemic index to express the degree of hepatic disorder.

A comparative study of the blood pressure and glycemic responses to epinephrine and ephedrine was made by Rodoslav and Stoicescu.[4] Their conclusion was that ephedrine causes the same blood pressure and blood sugar variations as epinephrine, but that its effects on the blood pressure are more enduring. In a group of thirty-four psychotic patients, Kanner [15] studied the epinephrine blood pressure changes. He found that all of the dementia praecox patients showed vagotonic reactions, and he made the statement that the degree of vagotonia did not depend on the type of dementia praecox but on the degree of emotional indifference. He observed further that in five cases of manic-depressive psychosis typical sympathicotonic reactions were elicited.

Not all writers are in agreement regarding the existence of vegetative tonus as elicited by the pharmacologic tests. Danielopolu [16] stated that many cases, classified by pharmacodynamic tests as vagotonia or sympathicotonia, are in reality of an amphotonic group with but temporary predominance of one or the other system controlling the heart.

12. Brill, S.: Glycogenolysis Due to Epinephrine in Hepatic Disease, Arch. Surg. **18**:1803 (April) 1929.

13. Kotschneff, Nina: Vollblutzuckergehalt verschiedener Gefässgebiete und seine Verteilung auf Plasma und Formelemente unter normalen Verhältnissen und bei Insulin- und Adrenalineinverleibung nach Versuchen an angiostomierten Hunden, Arch. f. d. ges. Physiol. **219**:407, 1928.

14. Kugelmann, B.: Das Verhalten der Adrenalin-Blutzucker-Kurven bei Erkrankungen des Leberparenchymus, Klin. Wchnschr. **8**:75, 1929.

15. Kanner, L.: The Adrenalin Blood Pressure Curves in Dementia Precox and the Emotional Psychoses, Am. J. Psychiat. **8**:75, 1929.

16. Danielopolu and Carniol: The Atropine Test and Orthostatic Tachycardia in Examination of the Nervous System of the Heart, Arch. d. mal. du coeur **16**: 161, 1923.

Langfeldt,[17] after investigating the sympathetic tonus of a large group of patients with dementia praecox and normal persons, stated that the pharmacologic tests alone were no gage of the permanent tonus of the sympathetic system. He found variations in the predominance of one or the other system in the same person in a quiet or an excited phase. It is acceptable that an existing affectless or an emotionally indifferent state is not of sufficient intensity to endure through a period of episodic excitement with its accompanying sympathetic discharge. Langfeldt found, nevertheless, definite signs of vagotonia in the catatonic group. Northcote,[18] after an investigation of the autonomic system in fifty cases of dementia praecox, stated that the action of pharmacologic substances is influenced by factors other than the state of the sympathetic nervous system and believed that pharmacodynamic tests should not be relied on as tests of the activity of the autonomic nervous system. Ganter [19] criticized the terminology so frequently used, asserting that the diagnoses of sympathicotonia and vagotonia are far too readily made. He found no value in functional pharmacodynamic tests since none, he believed, is capable of determining the actual tonus of the sympathetic system itself but only its effects on organs in which the sympathetic terminates. Sierra,[20] in an evaluation of pharmacodynamic tests in psychiatry, found no connection between them and mental disease. Kylin [21] tested a number of patients and normal persons belonging to both the sympathicotonic and vagotonic groups by administering epinephrine subcutaneously and found that true vagotonic persons reacted by a primary lowering of blood pressure, and sympathicotonic persons by an exaggerated rise. He linked these neurovegetative responses with the calcium-potassium ratio of the serum. Dressel [22] also investigated a number of normal persons and patients of both groups; he found a rapid rise of blood pressure attaining a height of from 50 to 60 mm. of mercury in the sympathicotonic group in response to 1 cc. of a 1:1,000 epinephrine solution administered subcutaneously. In the patients with mild vagotonia he

17. Langfeldt, G.: The Sympathetic System with Special Regard to Dementia Praecox, Norsk mag. f. lægevidensk. **86**:1, 1925.

18. Northcote, M. L. M.: The Clinical Investigation of the Autonomic Nervous System in Fifty Cases of Schizophrenia, J. Ment. Sc. **75**:114, 1929.

19. Ganter: So-Called Vagotonic and Sympathicotonic Symptoms, München. med. Wchnschr. **72**:1411, 1925.

20. Sierra, A. M.: Physiologic Tests in the Insane, Semana méd. **1**:3, 1923; abstr., J. A. M. A. **80**:967 (March 31) 1923.

21. Kylin, E.: The Epinephrine Test, Ztschr. f. klin. Med. **103**:233, 1926; abstr., J. A. M. A. **87**:211 (July 17) 1926. The Adrenalin Reaction in Cases of High Blood Pressure, Zentralbl. f. inn. Med. **43**:329, 1922.

22. Dressel, K.: Disease of the Vegetative System, in Spezielle Pathologie und Therapie inner Krankheiten, Berlin, Kraus & Brugsch, 1923, vol. 10.

obtained a slow rise of blood pressure; in the pronounced vagotonic group, a primary fall. Büchler [23] stated that all dementia praecox patients were vagotonic and all manic-depressive patients sympathicotonic. Kanner [15] believed that the epinephrine blood pressure curves are of such value as to be of use as a routine diagnostic procedure in psychiatry. Claude and his co-workers [24] made numerous observations of venous tension in mental disease. They found some cases of melancholia, dementia praecox and other psychoses showing a high venous pressure, with an increase to double the normal pressure in stupor and profound depression, and with signs of slowed circulation. The venous hypertension, they concluded, seemed to be connected with functional failure of the myocardium and with disturbances of the endocrine glands or of the vegetative nervous system.

TECHNIC

The subjects used were: ten patients with manic-depressive psychosis in the manic, depressed or mixed phases; ten with well established cases of schizophrenia of the catatonic, hebephrenic and simple types; five normal controls, and a more or less heterogeneous control group made up of patients with involutional psychoses, psychoneuroses and somatic disease. The patients in the schizophrenic, manic-depressive and normal control groups were all known by recent examinations to be free from systemic disease. The four groups were made up of six men and twenty-nine women, ranging in age from 19 to 52 years.

Classification of Cases Studied

Manic-depressive		10
Manic	4	
Depressed	3	
Mixed (agitated depression)	3	
Schizophrenia		10
Catatonic	4	
Hebephrenic	3	
Simple	3	
Normal controls		5
Other controls		10
Involutional melancholia	3	
Psychoneurosis (diabetes)	1	
Posttyphoid mania	1	
Obesity (hypertension)	1	
Pituitary dystrophy	3	
Postoperative myxedema (benign stupor)	1	

The technic was as follows: The blood pressure was taken after the patient had been in a recumbent position for twenty minutes. This was recorded as the basal blood pressure from which a basal pulse pressure was computed. All patients had abstained from food for a period of fifteen hours preceding the test. A specimen of 10 c.mm. of blood was then taken from a small puncture wound in the

23. Büchler, P.: The Vegetative Nervous System in Mental Disease, Orvosi hetil., 1921, vol. 65, no. 22.

24. Claude, H.; Targowla, and Lamache: Variations of Venous Tension in Mental Disease, Presse méd. **34**:1193, 1926; abstr., J. A. M. A. **87**:1689 (Nov. 13) 1926.

finger. The drops were obtained from the capillary circulation by rhythmic compression at, or proximal to, the distal phalangeal joint. Care was taken not to express the drops forcibly, thereby preventing adulteration of the specimen by tissue juices. Two specimens were taken of this fasting blood. All blood sugar estimations were done by the Hagedorn and Jensen [25] method. Thirty milligrams of a

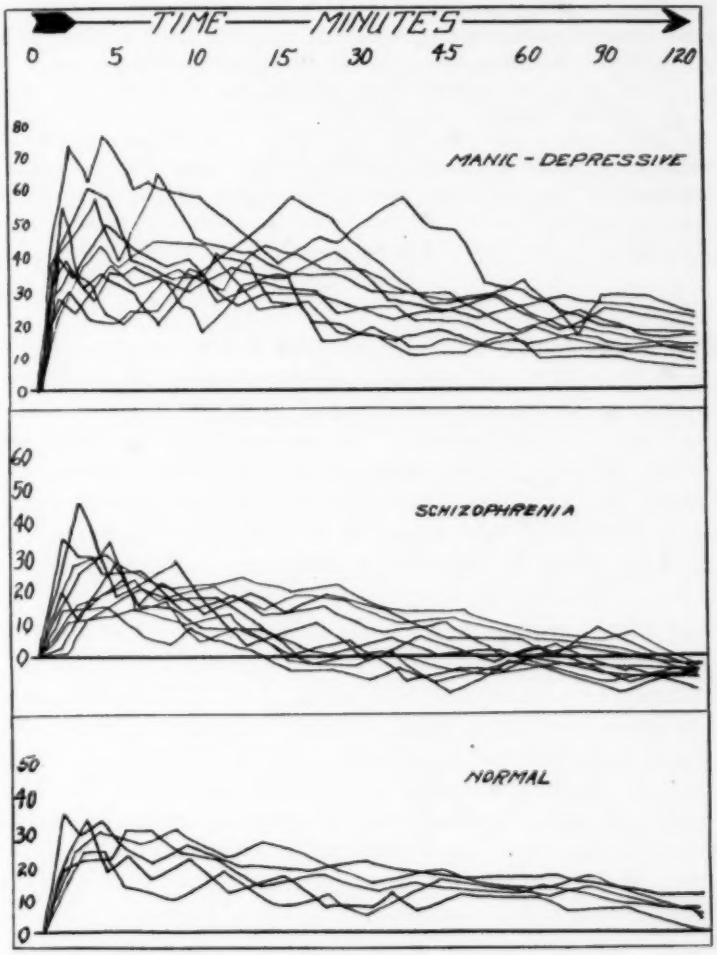

Chart 1.—Individual pulse pressure curves showing the variations from the basal pulse pressure values in the two psychotic groups and the normal controls.

1 per cent aqueous solution of ephedrine hydrochloride was injected intravenously and 10 c.mm. blood specimens were taken at five, ten, fifteen, thirty, forty-five, sixty, ninety and one hundred and twenty minutes for blood sugar determinations.

25. Hagedorn and Jensen: Investigations on the Blood Sugar in Man, Copenhagen, Hansen, 1923.

The pulse rate and blood pressure were taken every minute for four minutes, at two minute intervals for twenty minutes, every four minutes up to the hour period, and then every ten minutes to the limit of the two hours. Other observations were made from time to time concerning the activity of reflexes, emotional state, symptoms of cardiac embarrassment, etc., but no attempt was made to record accurately these observations. Charts were made for each patient, recording pulse pressure changes, systolic blood pressure rise, pulse rate alterations and blood sugar variations from the normal fasting level.

Pulse pressure variations were taken as the most expressive value in all the groups. A record of the systolic blood pressure rise alone does not take into account the diastolic changes. As a matter of fact, the systolic rise closely paralleled the pulse pressure variations, showing that the diastolic rise was concomitant with the systolic. Pulse pressure is assumed to be a more valuable expression of the magnitude of the ventricular contraction against the increased peripheral resistance, and therefore a more accurate expression of the compensatory power of the myocardium and the degree of stimulation of the sympathetic by the drug.

COMMENT

Blood Pressure Responses.—The manic-depressive group showed a pronounced rise of blood pressure; in several cases, the systolic value was well over 200 mm. of mercury and the pulse pressure attained a value of 80. The decline from the maximum at the three minute period was gradual and the elevation was well sustained throughout the two hours. At the end of the two hour period, the pulse pressure remained at about 15 mm. above the basal pulse pressure value. The schizophrenic group responded by a milder rise to a height of 30 mm. above the basal pulse pressure, and then fell quickly to a point below the basal pulse pressure value. The normal control group showed a response midway between the two psychotic groups. The marked rise of pulse pressure in the affective group shows that caution must be taken in the use of such a drug. Patients with cardiac disease, angina pectoris or arteriosclerosis or those past middle life should be excluded.

Some of the factors giving rise to such well marked differences have been previously discussed, but at this point another factor might be mentioned. Lewis [26] has shown that an aplastic cardiovascular system often exists in patients with dementia praecox and a large cardiovascular system in manic-depressive patients coming to necropsy. Trentszch [27] has made clinical application of this difference in anatomic

26. Lewis, N. D. C.: The Constitutional Factors in Dementia Precox, New York, J. Nerv. & Ment. Dis. Monograph Series, no. 35, 1923; Is There Fundamental Similarity in the Pathological Processes Which Occur in the Extraneural Systems of the Body? Heredity in Nervous and Mental Disease, A. Research Nerv. & Ment. Dis. Proc. **3**:190, 1923.

27. Trentszch, P. J.: Circulatory Ratings in Mentally Defective Adolescent Children, Am. J. Psychiat. **5**:593, 1926; The Determination of Possible Psychotic Trends in Adolescence by a Modified Circulatory Rating Test, South. M. J. **18**: 258, 1925.

structure in a circulatory test applicable to psychotic patients. He found that 82.6 per cent of the hebephrenic and catatonic patients give a low rating in the clinical test, while 88.8 per cent of the manic-depressive patients give a high rating. The relation of Trentszch's observations to the results under consideration suggests that the responses of the neurocirculatory system to the intravenous administration of ephedrine offer a basis for a controlled clinical diagnostic test. In none of the patients in the schizophrenic group did we find the typical vagotonic reaction obtained by some investigators employing epinephrine.

The slowing of the pulse rate which we observed in a number of the manic-depressive cases is doubtless due to the dose of the drug

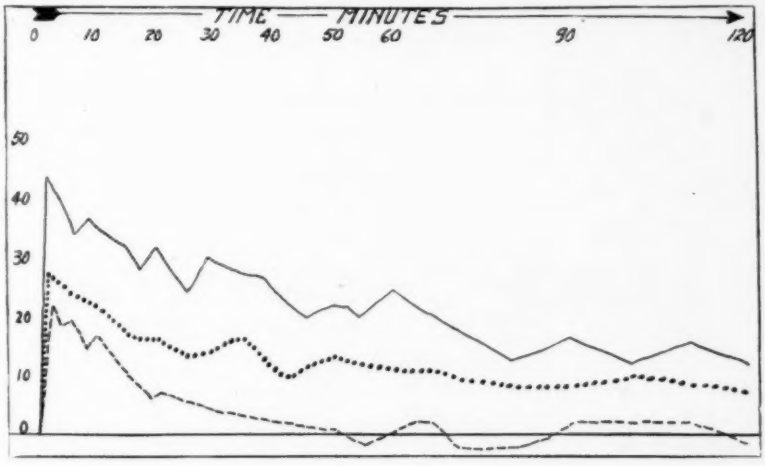

Chart 2.—Average pulse pressure variations from the basal pulse pressure values in the manic-depressive (solid line), schizophrenic (dash line) and normal control (dotted line) groups. The time factor is two hours and the pulse pressure increase is expressed in millimeters of mercury.

employed, one which in the manic-depressive patients was quite beyond the physiologic limits of the affectively sensitized sympathetic. The enormous rise in the arterial tension induced by the vasoconstrictive action of the drug increased the peripheral resistance to such a degree that it might have acted as a mechanical obstacle to the quick contraction of the ventricles (Cannon). This would have overcome the natural action of the drug to accelerate the heart rate. Such a condition may likewise prevail in the epinephrine experiments in which the apparently paradoxical slowing of the heart rate was attributed by

Guillaume [28] (quoting Danielopolu) to a simultaneous vagus and sympathetic stimulation. The assumption is that although the dose employed is of moderate size for normal persons, it is beyond the physiologic limits of the affectively sensitized sympathetic of the manic-depressive

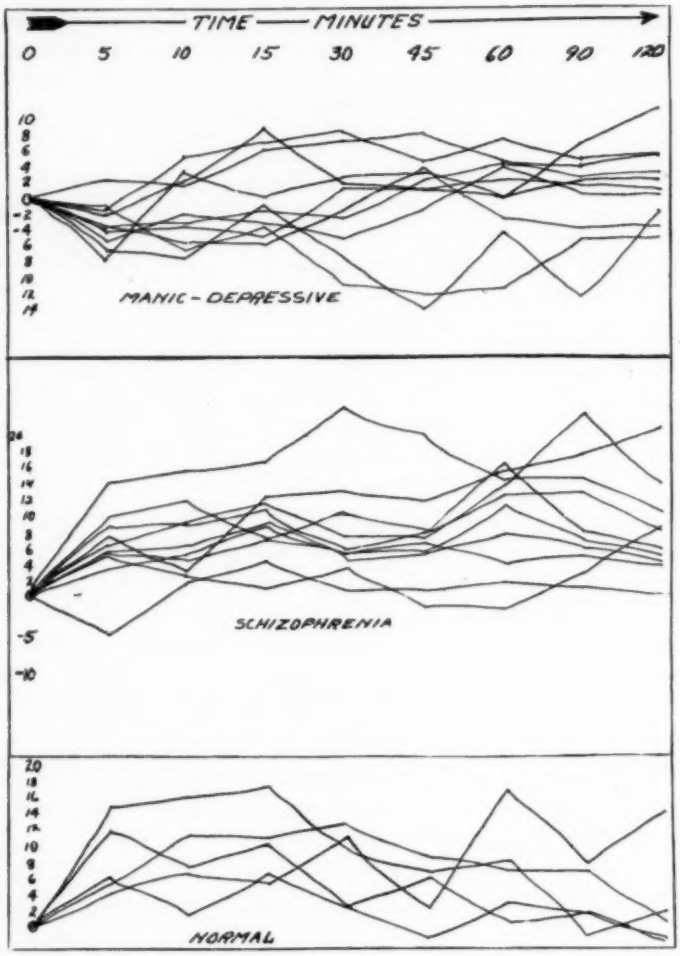

Chart 3.—Individual blood sugar curves showing the variations from the normal fasting levels in the two psychotic groups and in the normal controls. The time factor is two hours, and the blood sugar changes are expressed in milligrams per hundred cubic centimeters.

patient, and in the schizophrenic patient it is of sufficient size to produe only a mild physiologic action.

28. Guillaume, A. C.: Le sympathique et les systèmes associés vagotonies, sympathicotonies, et neurotonies, Libraires de L'Académie de Médecine, Paris, Masson et Cie, 1928.

Blood Sugar Reactions.—Blood sugar variations likewise result in well marked differences between the blood sugar curves of the manic-depressive, schizophrenic and control groups. The schizophrenic patients respond by a rapid rise, reaching a maximum at fifteen minutes, with a sustained elevation. The normal subjects showed somewhat the same type of diphasic curve as that obtained by Rodoslav and Stoicescu.[4] The manic-depressive curve bears a resemblance to the curves that Brill [12] and, later, Kugelmann [14] found in parenchymatous hepatic degeneration. The manic-depressive blood sugar curves show an initial drop below the fasting level, a slight rise at the fifteen minute period and then a continued fall to the end of the two hours. This deviation from the normal is difficult to understand since a function of the sympa-

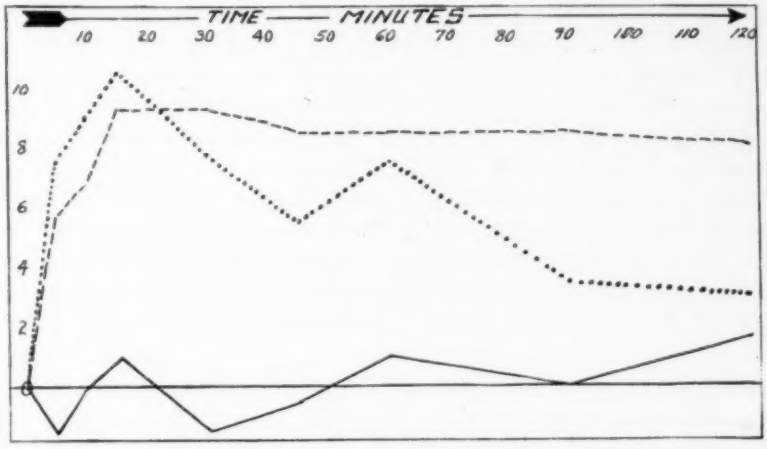

Chart 4.—Average blood sugar variations from the normal fasting level, expressed in milligrams per hundred cubic centimeters of blood. The value for the normal group is represented by the dotted line; that for the manic-depressive, by the solid line, and that for the schizophrenic, by the dash line. The time factor is two hours. All values reach a maximum at the fifteen minute period. Note the sharp initial fall and the markedly delayed mobilization in the manic-depressive group.

thetic is to mobilize the glycogen of the liver. It is possible that the glycogen store in the liver is somewhat depleted, that the affective disturbances serve constantly to activate the sympathetic, and that in response to the continuous flow of impulses the glycogen store in the liver becomes reduced? [29]

Controls.—The normal control group showed a rapid rise in pulse pressure which attained an average value of 28 mm. of mercury with a

29. Devine, H.: Recent Advances in Psychiatry, Philadelphia, P. Blakiston's Son & Co., 1929.

gradual decline extending over the two-hour period. At the end of this time it still remained slightly elevated. The average normal pulse pressure curve lies midway between those of the manic-depressive and schizophrenic patients.

The other control group showed varying curves and no degree of consistency could be demonstrated. Two of the three involutional cases responded with an exaggerated rise in pulse pressure, while the third showed a pulse pressure curve similar to the schizophrenic. The patient with hypertension and obesity, also suffering from a profound depression, reacted with a tremendous increase in arterial tension—a rise regarded by the examiners as dangerously high. In the involutional cases, the authors observed manifestations of cardiovascular disturbances evidenced by arrhythmia, dyspnea, and precordial pain, and regarded these reactions as unfavorable. We excluded the involutional types from our investigation because of the danger of unfavorable cardiovascular reactions. It is interesting and of some significance that the two patients with pituitary dystrophy, otherwise normal (non-psychotic), reacted with blood sugar curves closely paralleling those of the schizophrenic patients. The patient in a "benign stupor," which followed subtotal thyroidectomy and a resultant mild hypothyroidism, reacted with blood sugar and pulse pressure changes identical with those of the schizophrenic group. The psychoneurotic patient with mild diabetes ("potential diabetes" according to the dextrose tolerance tests) showed blood pressure and blood sugar responses identical with those of schizophrenia. The patients with posttyphoid mania reacted similarly to those with manic-depressive psychosis, but manifested untoward signs during the test. One catatonic patient with a clearcut pituitary syndrome reacted with typical schizophrenic blood sugar and pulse pressure changes.

SUMMARY AND CONCLUSIONS

Ephedrine hydrochloride, in our small series of cases, administered intravenously produced a tremendously greater blood pressure rise in the manic-depressive patients than in the schizophrenic or normal group. The structural peculiarities of the cardiovascular system of manic-depressive patients furnish an anatomic basis for interpretation of this greater circulatory response compensatory to stimulation by the drug.[20]

Ephedrine hydrochloride, given intravenously, produced in the manic-depressive group an average blood sugar curve showing an initial fall below the fasting level, a temporary rise reaching a maximum at fifteen minutes, and a secondary fall below the fasting level with a delayed rise toward the end of the two hour period. In the schizo-

phrenic group the same dose of the drug produced a marked elevation of blood sugar, attaining a maximum at the fifteen minute period which was sustained throughout two hours. In the normal person, the curve is diphasic—a sharp rise, slight fall and secondary rise, succeeded by a gradual fall toward the normal fasting level. That there exists a disordered carbohydrate metabolism in psychotic patients has been noted in numerous investigations. Bearing in mind the work of Brill,[12] Kotschneff [13] and Kugelmann,[14] one wonders if there is any possibility of a functional hepatic insufficiency in manic-depressive conditions. Could the increase of the sympathetic irritability bring about a release and a resulting depletion of the glycogen store in the liver? There is a similarity of the blood sugar curves obtained in our schizophrenic group to the curves obtained by us in persons suffering from evident endocrine imbalance, three cases of pituitary dystrophy, one of hypothyroidism, and one of mild diabetes. Such a resemblance raises the question as to whether endocrine dysfunctions have anything to do with the physiologic response in dementia praecox.

The indications seem to be that the manic-depressive patient shows a hyperirritability of the sympathetic, which we would interpret as an affectively conditioned sympathetic hypertonus, a reaction pattern fixed in the neural organization by habitual emotional impressions. The schizophrenics show a relatively inert sympathetic system as estimated by ephedrine stimulation. None of the typical vagotonic reactions, as elicited by some investigators employing epinephrine, was demonstrable with ephedrine.

Definite conclusions from the investigation of such a small number of patients are not warranted. The results obtained are subject to a variety of interpretations. It appears that intravenous ephedrine administration offers a basis for a controlled neurocirculatory test and for a physiologic distinction between affective and schizophrenic reaction types. We hope that this paper may afford suggestions for further work by other investigators with a larger series of cases in an endeavor to confirm or disprove our observations.

Clinical Notes

A UNIQUE TYPE OF SPEECH DISTURBANCE IN EPIDEMIC ENCEPHALITIS*

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The common causes of disturbance in the production of voice tone do not seem to account satisfactorily for the case that is here reported. This article attempts to describe a form of atonic and "asynergic" dysphonia possessing characteristic peculiarities of its own, but similar to those in a case I published in a previous paper.[1]

REPORT OF CASE

History.—C. S., a farmer, aged 38, complained of difficulty of speech that had existed for three years. Previous to six years before, the patient had been well. At that time he had the "flu," with fever, sore throat, headache and malaise, and he saw double for about ten days. After this brief illness he resumed work without unusual difficulty. About three years before examination, he experienced a slowness of speech which became progressively worse, and he began to suffer with insomnia. About one year prior to examination, his finger and arm movements, as well as mastication, became slow, and speech became deranged.

Physical Examination.—The patient was fairly well nourished; his height was 64 inches (132 cm.) and his weight 125 pounds (56.7 Kg.). He was without apparent deformities, except that over the malar prominences there was a pronounced telangiectasia. The facial expression was fixed and masklike, and the facial skin was oily. The hands were held in a fixed attitude, but adiadokokinesis was absent, and the grips were good. The pupils were symmetrical and equal in size, and they reacted to light and in accommodation; the eyegrounds and visual fields were normal; there was no nystagmus. The power of the arms and legs was good. There were some cog-wheel rigidity of the muscles of the neck and arms, and coarse tremors of the tongue and hands which increased with fatigue; the Aschner sign was present, and sialorrhea was marked. The muscles of the back and chest were held rigid and fixed, but on deep respiration they seemed to move unhindered. The gait was slow, but without spasticity or ataxia. The sense

* Submitted for publication, July 15, 1931.

* From the Department of Neurology and Psychiatry (Dr. H. Douglas Singer), Research and Educational Hospitals, University of Illinois College of Medicine.

* The case reported was presented before the Clinical Conference of the Research and Educational Hospitals, University of Illinois, College of Medicine, on Nov. 30, 1930.

1. Olkon, D. M.: Vocal Myasthenia of Postencephalitic Origin, Arch. Neurol. & Psychiat. **24**:570 (Sept.) 1930.

of position and deep sensibility were present. All mucous reflexes were present, and the pharyngeal reflex was prompt. The deep reflexes were lively and equal on the two sides. The abdominal, suprapubic and cremasteric reflexes were prompt. Babinski, Oppenheim, Gordon and Chaddock signs were absent. The oculocardiac reflex was markedly irregular, with long pauses and a marked reduction in amplitude, suggestive of a disturbance in vessel wall tonus. Galvanic and faradic stimulation of the muscles of the face, pharynx and lips produced normal reactions. All sensory reactions were normal.

The temperature, pulse rate, respiration, blood pressure, lungs, heart, abdomen, liver and kidneys were normal. The basal metabolic rate was plus 26 per cent. The capillary microscope showed marked atonicity of the microscopic vessels, suggestive of a grave interference with capillary function. The blood and spinal fluid appeared normal with all laboratory tests.

Speech.—Since there is no standardized way of describing variations of speech as to tonal quality, pitch and duration, and since there is no standardized acceptance of variations other than those described in disorders of speech incident to paralysis, paresis or motor interferences with the speech mechanism due to specific organic diseases, it becomes necessary to resort to a description employing other than the usual terminology.

In this patient, as the day progressed, the speech became whisper-like, barely audible and very slow, but without imperfections in the pronunciation of syllables and without scanning. The voice was lacking in energy, sounding like a weak blowing through a wide hollow tube. The speech muscles were in a state of fixity; the lips, facial muscles, tongue and pharynx barely moved, and the words came as if the larynx pushed them through the nose and between the teeth with a complete loss in tonal pitch. Hence, the term dysphonia was selected because of deranged vocalization, a kind of verbal disequilibrium. I am using the term dysphragic and dysphonic asynergia, realizing their unorthodox use, but since a single term did not suffice as a classification, I took the liberty of calling this particular speech disorder a dysphragic and asynergic dysphonia.

Comment.—That the case described does not belong to the usual categories of speech disturbances can be seen from the following: the consonants c, p, w, k, ch, m and f and the vowels u, i, e, o and a were distinctly but slowly produced singly and in syllables. The nasal twang was observed to be due to the uvula dropping into the postnasal space owing to muscular atony, instead of to paresis.

I cannot consider that the changes were due to thalamic disturbances or supranuclear involvement of the palatal muscles, resulting in paralysis of the vocal cords (laryngoplegia). In hysteria, one frequently observes "aphonia," or "dysphonia," and hoarseness of voice, but these are here excluded. In inflammatory conditions and neoplasms of the larynx one may have aphonia or dysphonia, but in this case no local inflammatory changes were found, nor did the tonsils and adenoids play a part in the speech disturbance The vocal cords were examined in the otolaryngology department and were reported as "normal." They were observed at rest and during inspiration and expiration, as well as during phonation. There were no abductor or adductor paralyses, nor was the internal thyro-arytenoid muscle involved.

The oculocardiac reflex was instructive: after moderate pressure over the middle of the epigastrium below the xyphoid, the radial pulse became irregular, with prolonged pauses which did not return to "normal" for several minutes. The respiratory curve was also affected by this operation. It showed a flattened curve characteristic of respiratory tonus disturbance.

While this condition of dysphonia is, I believe, due to a diffuse encephalitis, it did not show focal involvement of the glossopharyngeal or vagus; nor did it point to sequelae of a cerebrovascular accident that may implicate the corticobulbar control of these nerves which, together with the other pyramidal fibers, may produce the clinical picture of pseudobulbar palsy with disturbances of speech, phonation, mastication and deglutition. On the other hand, striatal phenomena were much in evidence, such as the parkinsonian syndrome. There were also marked sympathetic disturbances: sialorrhea, hyperhidrosis, dilatation of the pupils, and persistent dermographia and the Aschner phenomenon.

All of these observations by exclusion and inclusion point to a high grade of disturbance of muscle tonus and vasomotor and sympathetic mechanisms, encephalitic in origin, without the apparent involvement of specific motor, sensory and neural concomitants.

25 East Washington Street.

News and Comment

TENTH INTERNATIONAL CONGRESS OF PSYCHOLOGY

First Announcement: 1. In accordance with the resolution at the Ninth International Congress of Psychology in New Haven, Conn., in 1929, the Tenth International Congress of Psychology will take place in Copenhagen, from Monday, Aug. 22, to Saturday, Aug. 27, 1932, inclusive. His Majesty, the King of Denmark, has consented to take over the protectorate.

2. Psychologists and men of kindred sciences may participate as active members of the Congress. In addition, other persons interested may be admitted to some of the meetings as passive members.

3. The fee for active members is 150 francs and for their ladies 60 francs. The fee for passive members is 60 francs.

4. The official languages at the Congress will be English, French, German and Italian.

5. The Congress will be divided into sections, according to the number and character of the papers to be read. Some common symposia, with specially invited lecturers, will also be arranged.

6. During the Congress social gatherings will be arranged for the active members and their ladies, and an opportunity will be given to see Copenhagen under capable guidance.

7. Reservation of accommodations during the Congress has been undertaken by the American Express Company.

8. In connection with the Congress, tours to psychologic institutions in neighboring countries have been planned. The Committee of the Congress has been informed that Professor Katz, Rostock, from the "Deutsche Gesellschaft für Psychologie" will be in charge of tours to German and Austrian institutes. Professor Katz will be pleased to supply any information on application.

For the National Committee:

EDGAR RUBIN,
Copenhagen K. Studiestraede 6.

Obituaries

CONSTANTIN VON ECONOMO

(BARON ECONOMO VON SAN SERFF)

1876-1931

The profession of medicine may well pause in the busy round of its activities to consider the loss that has been occasioned to science and humanity by the death of one of the most brilliant representatives of Austrian neurology—Constantin von Economo.

His early life was passed in Trieste, at that time a part of Austria, where he was born in 1876. His family was originally of Greek derivation but had lived for centuries in the vicinity of Trieste, and he was by education and association wholly Austrian. He received his preliminary education in the Volkeschule and Gymnasium in Trieste, but his further premedical instruction was carried on in Vienna. For two years he was seriously engaged in technical and mechanical studies. He maintained this interest throughout the remainder of his life, and it proved to be of the greatest value to him in his later active interest in aeronautics, for he was among the first in Austria to enter into the practice of aviation. He was a most enthusiastic aviator, often spending the hours between daybreak and the opening of the clinic or laboratory at the flying field. He was at one time the active president and later the honorary president of the Royal Aero Club of Austria. He received his medical education in Vienna under Obersteiner and Exner, and early in his medical career he acquired the penetrating interest in the anatomy and physiology of the brain which was to dominate his later activities. Graduating in 1901, he continued his psychiatric studies with Kraepelin in Munich, who was so impressed by his industry, personality and promise that he tried in vain to induce Economo to remain permanently in his clinic. Returning to Vienna, Economo became an assistant in Wagner-Jauregg's psychiatric-neurologic clinic, where he remained for ten years except for the interruption occasioned by the World War. In 1920 he was appointed professor of neurology and psychiatry in the University of Vienna. As a result of his world-wide renown, he was sought by many clinics, hospitals and universities to direct their neurologic activities. The opportunity to become the successor to Edinger in Frankfort was offered to him, as was also the distinction of being asked to follow von Monakow in Zurich, but he steadfastly declined these and other honors, preferring to remain in his well loved Vienna and carry on his

life work there. In 1928 he was invited to succeed Wagner-Jauregg as director of the clinic of neurology and psychiatry but declined, fearing that the responsibilities resultng from his acceptance of such a position would leave him but little time and strength to be devoted to the investigation of the brain to which he had dedicated his life.

Economo was most fortunate in being united in marriage with Princess Lili von Schönburg-Hartenstein, the daughter of one of Austria's most illustrious soldiers, who was his constant companion in the many expeditions to foreign lands which his fame and prominence

CONSTANTIN VON ECONOMO
(BARON ECONOMO VON SAN SERFF)
1876-1931

rendered necessary. Their life together was one of ideal companionship and mutual understanding, and not a little of his great accomplishment was due to her constant care and foresight for him.

Although truly Austrian in loyalty and devotion, Economo was essentially a man of the world and counted among his firm and faithful friends persons belonging to nations on opposing sides during the years of the war. With the arrival of peace, he again threw himself unreservedly into his scientific investigations but also labored untiringly to restore

friendly and intimate relations between the scientists of the formerly belligerant nations. Realizing that this could best be accomplished by fostering and encouraging personal contacts, he was enthusiastic in his support of the International Neurological Congress and gave of himself without stint in the effort to make it a success. Little did it occur to those who were associated with him last summer at the congress that they were enjoying his personality, his humor and his scientific spirit for the last time.

The illness to which he eventually succumbed first made its appearance about ten years ago, when he suffered from a coronary occlusion which enforced a considerable period of inactivity. Recovering from its effects, he gradually resumed his accustomed activities. After returning to his home from the congress this summer, and without premonitory symptoms of importance, he suddenly suffered from a coronary embolism, the effects of which were subsiding when symptoms of a cerebral thrombosis appeared, from the effects of which he never recovered, and he died at his home in Vienna on Oct. 21, 1931.

It is scarcely two years ago that Professor Economo delivered before the Section of Neurology and Psychiatry of the New York Academy of Medicine an address concerning his recently developed technic for the investigation of the brains of unusual persons. This personal contact with the section and its members left an enduring impress on all and disclosed the qualities that rendered him such an outstanding figure in contemporary neurology.

It is unnecessary to mention in detail the many scientific achievements that have crowned his assiduous investigations. His name will always be associated in the minds of physicians with his identification of the latest scourge that has passed over the greater part of the world, epidemic encephalitis. In the issue of May 10, 1917, of the *Wiener klinische Wochenschrift* Professor Economo presented the results of his clinical investigations of a new infectious epidemic disease which he nominated "lethargic encephalitis." In a report published toward the end of 1917, he described this disease as a polio-encephalitis disseminated in small areas throughout the entire nervous system but showing a predilection for the gray matter of the mesencephalon. The reaction of the nervous system and its mesodermal elements was described as a non-hemorrhagic, non-necrotic inflammatory response. A few months later its true infectious character was established by the experimental transmission of the disease to monkeys, with the production of similar pathologic characters. These results have been confirmed by other investigators, and the disorder has become familiarly known as Economo's disease. This brillant contribution established his reputation as a clinician and has made his name a household one throughout the

medical fraternity. The somnolence so characteristic of the disease interested him to such an extent that his investigative efforts during the past few years were focused on the attempt to identify the location of a center for sleep, and these studies were the subject of a lecture that he presented at the College of Physicians and Surgeons during his visit occasioned by the opening of the New York State Psychiatric Institute. Added luster has been thrown on his indefatigable spirit by the publication of his monumental atlas on "The Cyto-Architectonics of the Adult Human Cortex," begun in 1912 and completed in 1925, which is accepted as one of the most searching investigations and most convincing proofs of the individual character of the diverse regions of the cerebral cortex.

Born into a family of established position and independent financial status, Economo was accustomed throughout his entire life to comfort and luxury. The driving force of necessity that affords the stimulus to effort and achievement for the great majority of professional men never played any part in his development and training. His scientific discipline resulting in such signal successes was the product of a remarkable singleness of purpose and intensity of application. His accomplishments were the fruits of an impelling force of character and love of scientific medicine. The absence of economic necessity not only seemed to increase his sense of obligation and responsibility to his profession and his fellowmen but also afforded him larger opportunities, denied to many less advantageously situated, for service to the community and to the world at large.

It is difficult indeed to choose from his many outstanding qualities those which seem best to illustrate the many facets of his engaging personality. His kindliness, sincerity, frankness and helpfulness were perhaps the characteristics that most endeared him to his friends. His opinions were always charitable and his words those of encouragement, his actions were embued with the spirit of a sympathetic, sincere and devoted friend. His passing leaves many who feel that although their contacts with him were all too short and too infrequent, there did exist between them an enduring and a cherished bond of interest and of mutual regard. His death deprives neurology of an active investigator, a brilliant clinician and an inspiring leader and robs Austrian neurology of one of its brightest luminaries.

ALFONS JAKOB

1884-1931

A short severe illness removed one of the outstanding contributors to our knowledge of the pathology of the nervous system on Oct. 17, 1931.

Early in 1914, coming fresh from the laboratory of Alzheimer, Jakob was made the director of the Neuropathological Laboratory of the Staatskrankenanstalt Hamburg-Friedrichsberg. He was hardly settled in his new position when the War broke out, and he immediately responded to the call of the Vaterland and did not return until the end of 1918. He then plunged into the organization of a laboratory which has become famous throughout the world. He began the collection of material for student use, representing practically every known neurologic and psychiatric disease, collecting more than 7,000 lantern slides for lecture purposes. He eventually had a working staff of one medical assistant, three male technicians, one female assistant, a secretary and an artist.

Since the War, more than 75 physicians from all over the world have studied in his laboratory, and there have been published over 150 "Arbeiten" which Jakob personally supervised. The great number and excellence of the publications are evidence of his untiring energy and brilliance. Probably the first work that attracted attention to him was on secondary nerve tract degeneration in the spinal cord (1912). Despite the great strides in our knowledge of the glia, Jakob's work in Alzheimer's laboratory still remains a classic, and is used as the basis for all work on this subject. The effect of Alzheimer's influence was still evident in 1920, when Jakob published one of the most important contributions on endarteritis syphilitica of Nissl and Alzheimer. In 1923 appeared "Die Extrapyramidalen Erkrankungen." This is all the more remarkable when it is realized that despite the fact that Jakob was a laboratory worker, he still had an excellent grasp on the clinical phases of this immense subject. It need only be stated that today no work on extrapyramidal diseases appears without reference to this classic.

Shortly after the publication of this volume (1924), Jakob, by invitation of Columbia University, gave a very successful course of lectures in New York City. He spent five months in South America in 1928, giving a similar course of lectures.

In 1925, Jakob began to collect material for "A Pathology of the Nervous System," the first volume of which was published in 1927, and the second in 1929. The third volume is probably now in print. To state that these two volumes are the best works on this subject in any language is to put it rather mildly.

ALFONS JAKOB

1884-1931

Germany and the world lost a man and a scientist who will be difficult to replace. His profound knowledge and sterling qualities of character impressed every one who came in contact with him. His influence on his pupils erected for him a monument that will endure, not in stone or bronze, but in the memories of men in all countries.

We, his pupils, who have respected him during life, mourn him in death.

N. W. WINKELMAN.

Abstracts from Current Literature

THE LOCALIZATION AND PATHOPHYSIOLOGY OF THE CHOREIC MOVEMENT. F. E. P. MEYJES, Ztschr. f. d. ges. Neurol. u. Psychiat. **133**:1 (April) 1931.

There seems to be increasing opposition to the striatal localization of chorea, and Meyjes has set himself to determine whether striatal pathology has any significance or at least any predominating significance in the production of chorea, whether it is correct or whether important changes must be made in it.

There are several opposing theories that deny the striatal localization of the choreiform movement. These are: (1) The theory of Kinnier Wilson, who in a case of senile hemichorea found post mortem only a circumscribed atrophy of the upper part of the heterolateral gyrus postcentralis. All other regions of the cerebrum, cerebellum and striatum were intact. Wilson believed that this case is evidence against the striatal theory of chorea, and stated that the theory is pathogenetically false and pathologically misleading. (2) The theory of French clinicians (Foix, Hillemand, Vincent et al.). Foix stated that: (*a*) A disturbance in the system from the dentate nucleus to thalamus (superior cerebellar peduncle) can evoke a choreo-athetosis; (*b*) the latter can be caused by other lesions; (*c*) choreo-athetosis is not a sign of deficit of function of the putamen. Foix and Hillemand expressed the belief that chorea in thalamic lesions is a symptom of disturbances in the cerebellothalamic fiber system. Roussy explained the chorea in striatal lesions through the striatal connections with the thalamus. (3) The theory of Niessl von Mayendorf who expressed the belief that chorea is produced by a lesion of the ansa lenticularis. He found that the mesial fillet splits into two portions, the medial portion going to the external nucleus of the thalamus and the lateral portion, as the ansa lenticularis, to the pallidum and putamen, into the external capsule and further corticalward. In a case of mild post-hemiplegic hypertonia, with cerebellar movements in the right arm, he found a small focus at the point of division of the mesial fillet, particularly in the ansa lenticularis. (4) Others disagree with the striatal theory, because chorea and athetosis cannot be consigned to lesions in a definite tract or structure (Minkowski, Spatz).

Meyjes points out that it is the cases with large, gross lesions, chiefly of vascular origin, that have been responsible for casting doubt on the striatal theory. These have been responsible for the clinically negative cases with striatal lesions, and for the clinically positive cases without striatal lesions. Experimentally, there are only a few observations that support the striatal theory — those of Lewy on mice into which B. diphtheriae were injected, and those of Mella on monkeys treated with manganese in which lesions were found in the striatum and none in the cerebrum.

On the other hand, it is the cases of acute chorea, of chorea gravidarum and of chronic progressive chorea that lend support to the striatal theory. The cases of chorea with coarse vascular lesions constitute the weak point, therefore, in the striatal theory.

The significance of the clinically negative cases of chorea is hard to evaluate. It is not surprising that a focal lesion that destroys only a small part of the striatum and leaves much of it undamaged should not cause chorea. One cannot state with certainty how large a lesion must be to produce clinical symptoms. These depend on the size of the lesion, the acuity and type of process, diaschisis, etc. Also, one must not lose sight of the fact that in large striatal foci the internal capsule is injured, and one knows that severe injuries of the pyramidal tract cannot be accompanied by choreo-athetosis.

More potent arguments against the striatal theory are brought by the cases of chorea without striatal lesions. These cases are still very rare. They include: (1) The case of senile hemichorea of Wilson, already referred to. Meyjes calls

attention to the fact that Wilson seems to have disregarded entirely a small softening in the opposite thalamus. This softening was small, to be sure, but a focus of this sort, no matter how insignificant is of great import in this region. (2) The case of Niessl von Mayendorf. It is doubtful whether the ansa is significant for the production of choreo-athetosis, and the work of von Mayendorf on the mesial fillet has not been confirmed. Recent work of Kodama, on the other hand, confirms the earlier descriptions. (3) Cases of hemiballismus with lesions in the corpus Luysii. These have been frequently described and confirmed in recent years. (4) Chorea in thalamus lesions. It is rare in these cases that one can eliminate an indirect striatal injury. In two cases that Meyjes studied, there was a lesion in one instance in the lateral nucleus with the appearance of chorea, shortly before death, on the same side as the thalamus symptoms; in the second case there was a similar softening in the lateral nucleus of the opposite side. Usually, the chorea is overshadowed by the sensory symptoms in thalamic lesions. Spatz assumed, with the Vogts and Jakob, that the hyperkineses in thalamic lesions are due to an indirect functional disturbance of the extrapyramidal motor system. (5) The cases of chorea from lesions of the superior cerebellar peduncle (Bonhoeffer). In these the striatum is untouched. Recently, Bonhoeffer has described two cases of hemichorea caused by a tumor metastasis and tubercle in the subthalamic region. The foci had involved the substantia nigra, red nucleus and corpus Luysii, and in one case the superior cerebellar peduncle. Bonhoeffer called attention to the significance of this region for chorea, and denied the striatal theory of Vogt. (6) Chorea in lesions of the nucleus ruber (Halbau and Infeld). While the pathologic process in these cases spreads beyond the red nucleus, it leaves the striatal connections intact.

Similarly, cases of chorea with lesions limited strictly to the neostriatum are rare. These cases include one of Jakob with a ticlike chorea of one side of the face and at autopsy a small malacic cyst in the opposite head of the caudate; a case of Souques and Bertrand, with hemiparesis at 4 years of age, hemichorea and a circumscribed focus in the opposite putamen and caudate; the case of Vogt, with involvement of the striatum and a recent softening in the centrum ovale of both hemispheres, and the cases of beginning Huntington's chorea without psychic disturbances and with severe changes in the neostriatum but none in the cortex or elsewhere.

Meyjes reports a new case of hemichorea with localized striatal involvement. A woman, aged 76, showed on admission chorea involving the right foot and later the right arm, and died about six weeks after the illness began. Microscopic study showed atrophy of the left caudate and putamen. The entire left striatum was smaller than the right, especially in the anterior portions. There were small softenings in the left putamen. All other areas were normal. Meyjes believes it logical in this case to tie up the clinical manifestations with the anatomic observations. The atrophy of the striatum was probably of long standing, so that the recent softenings in the putamen were probably important in the production of the chorea.

The cases of symptomatic chorea in paresis and senile dementia are difficult to explain. Meyjes reports two cases of senile chorea with rather severe changes in the cortex and striatum. In senile chorea, therefore, there is, besides the lesions in the cortex, an affection of the striatum, which is greater than is found in usual cases of senile dementia without severe extrapyramidal motor symptoms. Cases of diphtheric chorea and chorea gravidarum may also be included among the symptomatic choreas. Cases of chorea in diphtheria show an exquisite striatal involvement. Cases of chorea gravidarum show an involvement of the striatum, but some have been reported with a more diffuse involvement.

Cases with gross lesions are therefore more or less not clear as to striatal involvement, but most of them favor the striatal theory of chorea. Of the symptomatic cases, the cases of chorea in diphtheria and of chorea gravidarum support definitely the striatal theory, the cases of senile chorea less so, and those of chorea in dementia paralytica still less.

Most important from the standpoint of localization are the cases of Sydenham's and Huntington's chorea. In acute Sydenham's chorea, the studies of Alzheimer, Lewy, Marie and Tretiakoff and others have shown that there is a selective involvement of the neostriatum. In the chronic progressive choreas there is also a striatal selectivity. The cases of Vogt and Jakob are particularly valuable, since they showed early Huntington's chorea without psychic symptoms and with striatal but no cortical involvement. The small cell striatal involvement seems to be supported by these cases of Huntington's chorea.

The cases of chronic chorea in which rigidity with loss of the chorea has developed later are instructive. Jakob reported such a case in which, in addition to the usual changes of Huntington's chorea, he found involvement of the large cells of the striatum and the zona reticulata of the substantia nigra. The latter, he thought, explained the rigidity. Spielmeyer objected to this view on the grounds that not enough is known about the functions of these areas to say that they cause definite clinical symptoms. To illustrate this he reported two cases of Wilson's disease that showed the changes found at necropsy in Huntington's chorea with relative intactness of the pallidal and large striatal cells. Meyjes reports further cases of Huntington's chorea in which hypertonicity has developed later, and finds that there is marked atrophy of the entire brain and striatum, as well as of the pallidum, with marked loss of small striatal cells, and less marked loss of the large striatal and pallidal cells. It appears as if the anatomic process in these "hypertonic" cases has developed with greater intensity and has involved the pallidum as well as the large striatal elements.

To return to the question of localization, then, it appears that for many forms of chorea the lesions in the striatum are a very important if not a necessary factor. In chorea minor, chorea in infection, chorea gravidarum and chronic progressive chorea the striatum is regularly affected, whereas negative cases in these diseases are either rare or never seen. The difficulty is that in all these cases there are other more diffuse changes which complicate the picture. The same may be said of symptomatic chorea. There are only three cases in the literature with focal involvement of the striatum. In chorea, a lesion in the striatum is very common, though it is not the only change.

The striatal theory of chorea would be untenable were it to state that "chorea rests on a lesion in the neostriatum." The striatal theory is untenable in this absolute sense, because there are cases of chorea on record without involvement of the striatum. If, however, one states that the neostriatal lesion is the most regularly recurring anatomic factor, which can produce the choreiform mechanism under certain complicated conditions, then the striatal theory appears to be correct. Furthermore, if, as Kinnier Wilson wishes, one were to look on chorea as a lesion not of a localized but of a very widely scattered system, the striatum would still be the most important central point in this system.

ALPERS, Philadelphia.

NEUROLOGIC SEQUELAE OF EPIDEMIC ENCEPHALITIS. M. RISER and PAUL MÉRIEL, Rev. d'oto-neuro-opht. **9**:297 (April) 1931.

This report, to the Fifth Congress of French Societies of Oto-Neuro-Ophthalmology, is a part of a symposium on the oto-neuro-ophthalmologic sequelae of epidemic encephalitis. The otologic aspect was discussed by Portmann and the ophthalmologic by Teulières and Beauvieux. No attempt is made to present a critical survey of the subject; only a clinical classification of the observed phenomena is offered. This study is based on 300 cases observed between 1919 and 1930, and on 100 cases occurring between 1915 and 1920, in which the patients have been reexamined. Sequelae are defined as "anatomic or clinical residual phenomena, without evolutive character, which follow an active lesion that has become stabilized." The virus of epidemic encephalitis may remain fixed in the neural axis for a long time and thus give rise to "prolonged forms," which are not true sequelae.

True sequelae are: (*a*) definitive paralyses of extrinsic or intrinsic ocular muscles;* (*b*) flaccid paraplegias in the form of transverse myelitis or pure spastic paraplegia (rare); (*c*) ordinary hemiplegia from foci of softening or hemorrhage; (*d*) permanent sensory disturbances of the thalamic or juxtathalamic hemialgic type; (*e*) internal hydrocephalus from blockage of the flow of the cerebrospinal fluid, causing a syndrome of cerebral tumor, with headache, vomiting and vertigo; (*f*) chronic disturbances of metabolism of water, fats and carbohydrates; (*g*) amyotrophic paralyses, localized in a muscle group; (*h*) deformities of the extremities in certain cases of parkinsonism from tendon retractions. The cases in which there is a relapse are not discussed. They usually end, after a free interval, in parkinsonism or other chronic dystonias.

The prolonged forms usually follow the acute stage after a free interval of several months or years. Their manifestations are varied, the most important being: (1) dystonic states, disturbances of the extrapyramidal motility; (2) disturbances of the great organic functions, neurovegetative and metabolic, and troubled sleep, accompanied by dystonias; (3) mental disturbances.

In each normal person there is a permanent tonus which never completely disappears. Based on this, there are distinguished a tonus of general posture that, ever changing, preserves equilibrium, and a tonus of segmental posture, which is expressed clinically by reflexes of posture. In epidemic encephalitis the dystonias may be classified as: (*A*) permanent dystonias, of which parkinsonism is the type, following static disturbances and exaggeration of the tonus of posture; (*B*) paroxystic dystonias, in which a clonic element intervenes, which results in involuntary choreic or spasmodic movements.

A. This group is characterized by disturbances of motility and station. Trembling belongs to the paroxystic dystonias, but is usually described with parkinsonism. A case showing marked permanent hypertonia of the neck muscles is described. Parkinsonism begins with trembling and rigidity. The aspect of the patient is characteristic: immobility of the face, slobbering, slowness and stiffness of movements and guttural laughter. In walking, the head, neck, body and arms are flexed, and the arms are held against the trunk. The patient takes short, quick steps. Gestures are few and, when made, are slow with stops and starts. Motor acts are interrupted and the attitude of the limbs is long maintained. In contrast, during active movements, the muscles are easily fatigued, as may be seen in pseudo-adiadokokinesis. In many cases, hypertonia and increase of tonus of posture are added to the muscular fatigue. Stiffness is more or less variable; it affects the extensors and flexors equally and is greatly diminished during sleep. In proportion to its degree, muscular contraction and relaxation become cogwheeled. The absence of trembling has been noted in some epidemics. In seven of the authors' cases trembling preceded the hypertonia and bradykinesis by from two to twelve months. It diminishes or stops during voluntary or automatic movements and during true static repose. The reflexes vary from one time to another, being influenced by the rigidity, the slow relaxation, fatigability and the patient's emotional state. Objective disturbances of sensibility are not a part of the syndrome. However, the relative frequency of pains in the neck, face and limbs must be remembered. They are often of thalamic or juxtathalamic origin. Porot has emphasized the importance of peripheral vasomotor dilatation and erythematous patches. The emotions can reinforce or inhibit the rigidity, slowness and loss of automatism. Complete repose and sleep diminish them. One patient became supple and normal during an attack of somnambulism, but immediately became rigid again on waking. Paradoxic hyperkinesis during the waking state has been noted. Certain complex acts can be performed, but only a given one, always the same. Psychic disturbances are almost never present. Froment regards dystasic rigidity as one of the most characteristic signs; while, in a normal person, a temporary reinforcement of the static tonus occurs from time to time and results in transitory rigidity, the parkinsonian patient, having partially lost static function, must constantly reinforce tonus. This causes muscular overwork and constant rigidity, with hyperthermia and disturbed muscular metabolism. The

intensity of the rigidity varies with the static attitude of the patient. In order to discover latent rigidity, Froment, Foix and Delmas-Marsalet devised tests of the static function and of reflexes of posture. Subvarieties of parkinsonism are: hemiparkinsonism, localized parkinsonian hypertonia, and monoplegic, paraplegic and akinetic or bradykinetic forms. The last are characterized by almost complete absence of hypertonia, slight increase of resistance to passive movements, slowness of motor acts and persistence of attitudes. This loss of automatism is the result of a deficit in certain central formations and not of a local lesion. Four per cent of the cases were of this type, not absolutely pure, and all have ended in classic parkinsonism. Minute investigation is required to recognize these obscure forms and an etiologic diagnosis is important. Rarely, subacute forms of parkinsonism may apparently end in recovery. In slowly progressive parkinsonism, without previous acute manifestations or occurring after a free interval, several eventualities are possible: (*a*) The syndrome becomes fixed, especially the hemiparkinsonian type. There were forty-six cases, of which thirty have been observed since from 1920 to 1924. Twenty-two appeared to be stabilized for several years but, in reality, have progressed slowly; eight have not changed. (*b*) Of one hundred cases of trembling and rigidity, in existence since 1920, ten have remained stationary; in sixty the rigidity and bradykinesis have increased, although the patients can still walk a little; thirty patients have become bedridden, absolutely rigid, emaciated and cachectic, and active movements are impossible. At times the cachectic state develops rapidly. In these patients, von Economo thinks there are lesions of the encephalic sympathetic centers. In a group of these cases with more hypertonia than trembling, the patients were emaciated and had bedsores, and insulin was of service. Twenty cases in the terminal stage have been studied. In one, Babinski's sign, with ankle clonus, and a predominance of contraction of the extensors, indicating pyramidal involvement, were present. No paralysis of the cranial nerves or objective signs of disturbances of sensibility have been found.

The question has been raised as to the relationship between certain prolonged forms of encephalitis and catatonic dementia praecox. In the present state of knowledge, the two syndromes must be regarded as distinct from each other.

B. Paroxystic dystonias are motor disturbances that determine abnormal but not fixed attitudes, to which a clonic element is added. There are sudden variations of tonus, and isolated or grouped muscle contractions, causing involuntary, stereotyped and complex movements. The elementary dystonias are curvatures of the trunk, torticollis and athetosis. Dysbasia lordotica is the most common. There were two such cases in the series, in one of which no hypertonia of the sacrolumbar muscles was found. In both cases the lordosis was absent in the recumbent position and became progressively worse as the sitting, standing and walking positions were assumed. These vicious attitudes have a complex pathogenesis: hypertonias or hypotonias of muscle groups, and perhaps alternations and intrications of one or the other. They are often accompanied by torticollis or more or less generalized torsions. Torticollis is usually isolated. The dystonia is overshadowed by spasmodic involuntary contractions of a muscle or a group of muscles. The contractions are executed slowly and irregularly and are not painful. The crises are induced by a voluntary contraction, the emotions, tonic reinforcement of postural attitudes, standing and walking. Repose suppresses the spasm in some cases. In six of fifteen cases, the spasms were as frequent and as intense in the recumbent position as during walking. At times the spasm may be inhibited by minimal antagonistic gestures. Barré thought that there were dystonic phenomena present between the crises, but in seven of the authors' cases none could be distinguished. In two cases with contraction of the right lateral muscle group, Laval and Rigaud noted labyrinthine hyperexcitability on the right side. The evolution of torticollis varies; it may remain isolated for a time and be followed by parkinsonism; the two may occur simultaneously, or it may remain pure for years.

In some cases the syndrome of decerebration has been noted. It is characterized by extreme extension of the trunk, neck and feet. It is most often permanent, but is intensified by positions that increase the tonus of attitude.

The syndrome of athetosis is characterized by slow and undulatory, stereotyped and involuntary movements. Rarely it is limited to the fingers, but usually the limbs are also involved. Neither sleep nor repose suppresses it, and it is made worse by voluntary acts, especially standing and walking. Large doses of scopolamine and morphine do not diminish the movements and they disappear only in profound general anesthesia. More complex cases, in which twisting of the limbs and trunk are combined with the athetosis, may occur. Such a case is reported.

Myorhythmias affect a muscle, a muscle bundle or a group of muscles. The contractions are rhythmic and constant in frequency for a given patient. Any muscle may be affected. They are akin to certain rhythmic athetoses or choreas. Signs of parkinsonism appear late, and the rigidity diminishes the number and intensity of the myoclonias and myorhythmias. Choreic movements are not uncommon. They may remain pure or be accompanied by signs of parkinsonism (rarely) or by athetoid movements.

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GLIOMA OF THE RETINA INCLUDING THE RESULTS OF STUDIES WITH SILVER IMPREGNATIONS. ROY R. GRINKER, Arch. Ophth. **5**:920 (June) 1931.

In this article an embryologic and histologic study of the retinal development is first outlined; with this the author correlates the formation of epithelial tumors of the retina. They may be considered as: those arising from the primitive retinal and ciliary body epithelium, the medullo-epitheliomas; those from the hypothetic bipotential indifferent retinoblast, the retinoblastomas (sometimes called retinocystomas), and those from the primitive spongioblasts or neuro-epithelium, the so-called neuro-epitheliomas. Each of these separate classifications is discussed from a histologic standpoint. In the discussion, the author refers to the literature as to previous opinions and to existing histologic descriptions.

In medullo-epitheliomas the cells are laid down in bandlike structures, the cells several layers thick, their nuclei lying in the portion of the cell closest to the interior of the band, but a protoplasmic border is present on either side of the nucleus. Degeneration of the cells is frequent, as evidenced by pyknotic nuclei. An external and an internal limiting membrane in the bands and lumina are present, and connective tissue stroma is found between the bands. Vesicles are formed which in shape and type of cell duplicate almost identically the structure of small embryonic retinal vesicles. Even an attempt at vitreous formation was noted within them. Certain lumina contain knoblike processes extending beyond the cells into the central cavity, resembling rods and cones. These were typical rosettes composed of primitive spongioblasts with fine fibrils arising from them. A moderate amount of connective tissue stroma lay between the columns of cells. These typical tumors are fundamentally composed of bands of columnar epithelium resembling the primitive medullary retinal epithelium, with evidence in the tumor of differentiation into retinoblasts and neuro-epithelium in the shape of rosettes, which will be discussed later, bipolar spongioblasts, ependymal cells and even adult glia.

Retinoblastomas: It seems that this type of tumor forms the vast majority of the retinal gliomas, and the usual descriptions found in the literature under descriptions of retinal glioma apply to this neoplastic growth. As introduction, the retinoblast is a hypothetic cell analogous to the medulloblast or bipotential cell arising from the medullary epithelium. It is bipotential in that subsequently it may form ganglion cells or adult glia. As the author states, on this hypothesis this type of tumor should contain evidences of an attempt to differentiate in either direction. They arise from the posterior part of the retina and even from the papilla. They are the only known neoplasms of glial origin that metastasize to distant parts and are of a high grade of malignancy. The tumor consists of small, round and polygonal, often carrot-shaped cells containing scanty cytoplasm and usually closely packed together. The nuclei are large and dark staining and have a definite chromatin network. Fine tail-like processes from one end of the

more elongated cells are found in rare instances. Intercellular substance cannot be seen except for a fine reticular stroma. Mitotic figures are most abundant in this tumor.

Some of the various authors quoted, especially Urra, have shown that by means of silver impregnations a most accurate description of a retinoblastoma is possible. This has been done. In his tumor (Urra) there were apparently three zones of tissue, which seemed to represent stages in the histogenesis in situ of the retinoblastic cells. The external zone was composed of cells with scanty cytoplasm and large, well developed argentophilic nuclei undergoing frequent simple mitoses. The cell shapes were lancet-like or pearlike, although fully rounded cells were also found. No reticulum could be seen, but there were numerous small-channeled capillaries composed of single layers of endothelial cells. In the outermost portions of the tumor, the capillaries were proliferating and mitoses of the tumor cells were frequent, but further inward, degeneration of the capillaries was more common and mitoses were less frequent. In the intermediate zone, the cells were more elongated, and their tail-like processes tended to become attached to the wall of a blood vessel in the form of a sucker foot. In the innermost zone, typical adult astrocytes, with well developed sucker feet and two or three processes containing fibrils, were seen. Thus a local histogenesis in this tumor was described from the retinoblast to the spongioblast and adult astrocyte. Bipolar cells with delicate processes representing spongioblasts as well as a few more adult astroblasts and astrocytes might be present.

In this tumor, degenerative changes, such as necrosis, fatty degeneration, calcification and even hemorrhages, were frequent. The cells then undergo differences in staining. Numerous large phagocytic cells can be found, as well as other changes characteristic of degeneration. The confusion in the nomenclature of this type is rather distressing. They might properly be called retinoblastoma gliomatosum. Cattaneo called them retinomas, while Mawas termed them retinocystomas. The author believes the term retinoblastoma to be most appropriate to the type and stage of differentiation of the neoplastic cells.

Neuro-Epitheliomas: In this type of tumors, the chief characteristic is the formation of true rosettes, though the rosettes occur in tumors of more primitive structures as well. In discussing neuro-epitheliomas, the author falls back on Fuchs' original classification (1908), wherein he divided them into benign adenomas and malignant tumors. The benign tumors that he described were probably neuro-epitheliomas, which have a glandular appearance because of their rosettes. Associated with their more advanced position in the histogenetic series, these tumors are relatively less malignant. The same neuro-epithelial structures may appear in senile excrescences of the ciliary body, and they apparently have little tendency toward growth. Numerous typical rosettes have also been observed in intra-ocular infections involving the ciliary body. Furthermore, Wehrli, Fuchs and others found rosettes pinched off from the retinal epithelium in microphthalmia associated with developmental defects of the brain. Wehrli expressed the belief that folding of the retinal epithelium and pinching-off of rosettes takes place rather frequently, and that birth trauma and hemorrhages stimulate them into rapid malignant growth.

Fuchs' malignant tumors include those that completely imitate the embryologic retina (diktyoma), those that are undoubtedly medullo-epitheliomas and the less completely imitative tumors, probably retinoblastomas and neuro-epitheliomas.

The author used a technic of silver impregnation for his study of these various gliomas. In his studies, rosettes and pseudorosettes were both demonstrated. The cell membranes form the internal limiting membrane of the rosette. Colloid or hyaline material may be present in the cavity. Fine delicate cilia-like processes project through the internal membrane, and from the outer pole of the cell there projects a fine indistinct tail-like process. The greatest part of the cytoplasm exists between the nucleus and the internal limiting membrane. No external membrane can be found, and mitotic figures are abundant. Between the rosettes are many small round cells with scanty cytoplasm and dark-staining nuclei, apparently retinoblasts. Many elongated spongioblasts, their fine processes attached to

blood vessels, also lie between the rosettes and numerous newly formed blood vessels. The walls of the blood vessels are thickened and show hyaline degeneration. Hemorrhages, as well as degenerated areas with poorly staining cells, are present. The close resemblance, here as well, of the spongioblasts to normal rods and cones is marked. The cell bodies with their processes are very similar to the normal corresponding position of the rod cell. This seems to indicate rather well that the normal rods and cones are definitely a sensory epithelium and not ganglion cells, and are derived from a portion of the retinal epithelium corresponding to the primitive spongioblasts of the brain. Bailey and Cushing correctly called these tumors spongioblastoma primitivum retinae. The degenerative cells showed well with the silver impregnation technic. The extreme thickening of the blood vessels in the degenerative areas, probably the cause of the degeneration of the cells themselves, was also remarkably well shown. The individual cells and their processes could be readily seen. In the illustrations included in the article, this is convincing. It was only through this special technic that the cell processes could be so well seen. The study of the astroblast (a cell somewhat more developed than the spongioblast, but itself a precursor of astrocytes), with its small rounded body, considerable cytoplasm and definite processes, was well worked out. A similar study of the astrocytes themselves, of their different position in relation to the blood vessels, of the larger, more angular shape of the cell body and of the changes in their cytoplasm was also possible. Other important detailed points were also studied: additional cells, probably primitive spongioblasts and oligodendroglia, other arrangements of cells within the tumor mass, detailed changes in the vessel walls and accurate information as to the formation of the rosettes.

In the summary of the article, the author recapitulates as follows: The medullo-epitheliomas consist mostly of primitive retinal epithelium which persists in adult life as ciliary epithelium and from which these tumors arise, and also of neuro-epithelium and retinoblasts. Retino-blastomas, on the other hand, are composed chiefly of retinoblasts. In them, evolutionary states in the histogenesis of adult retinal glia have been found, but no cells of the ganglion series. In the neuro-epitheliomas, spongioblasts are found in a rosette-like arrangement. In addition, astroblasts, astrocytes and oligodendroglia, all normally derived from the neuro-epithelium, are also found.

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EXPERIMENTAL DEMONSTRATION OF THE MORPHOLOGIC AND FUNCTIONAL PROPERTIES AND THE MESODERMAL NATURE OF THE MICROGLIA. I. COSTERO, Ztschr. f. d. ges. Neurol. u. Psychiat. **132**:371, 1931.

Knowledge of the microglia is dependent on the researches of Rio Hortega (1919-1921), who first discovered these elements. According to Rio Hortega, the microglia develops from polyblasts or embryonal cells of the membranes of the brain in the later stages of embryonic development, and then penetrates into all parts of the brain in the days following birth. These cells assume round and pseudopodic forms in the course of their wandering, but later they branch out, assuming a form with a small dark nucleus surrounded by a scanty cytoplasm, giving off a few or many prolongations that branch richly, possess short spines, and end freely without anastomosing either with one another or with the neuroglia cells. The microglia represent the reticulo-endothelial system of the nervous system and possess all the properties of this system: the ability to take up certain colloids and to phagocytose red cells and degenerated cell products. Besides this the microglia play an important rôle in all inflammatory and necrotic processes of the nerve tissue, and assume the form of rod cells or gitter cells. The gitter cells are exclusively of microglial and histiocytic origin.

These fundamental concepts of Rio Hortega concerning the microglia have been in the main accepted. The origin of this element is a matter of some dispute, and some investigators (Metz, Spatz, Jakob, Schaltenbrand and Bailey) have assumed an ependymal origin, while others have accepted the mesodermal origin

of these cells. Jakob believed that the microglia forms a part of the glia reticulum, which is composed of astrocytes and oligoglia. Schaffer looked on the microglia as a subtype of macroglia. Some investigators do not believe that the gitter cells have purely a microglial origin. They are said to develop also from endothelial and adventitial cells and monocytes. Pruijs believed that the oligoglia form gitter cells, and Jakob also accepted this view, believing that the oligoglia forms myeoloclasts and the microglia myelophages. Spatz and Metz opposed the idea that the microglia forms a part of the reticulo-endothelial system. Testa demonstrated that the microglia alone possessed the power of ingesting particles of pyrrole blue and lithium carmine. Other investigations of this property have given negative or unsatisfactory results. Bellavitis and Russell found, in experimental production of wounds, that the microglia ingested trypan blue. Castero has shown that only the microglia are capable of proliferating in vitro and of forming cultures that are conservable and can be used for forming new cultures. This fact has been used in the present study in order to determine the exact properties of the microglia. Since the method of explantation has been used on nerve tissues, all investigators have noted the ease with which the microglia proliferates in cultures. Harrison described cells in cultures of frogs' brain and cord which were filled with granules and which wandered all over the field. These cells were probably microglia cells. Burrows, Shorey, Olivo and others have described microglia in their cultures. It is possible that these elements may be fibroblasts, but since the microglia are the only cells capable of proliferating profusely in these cultures, they must be microglia.

Costero used chick, mouse, rat, rabbit, guinea-pig and human embryos in his culture experiments. The best results were obtained from the chick embryos. Gray matter was cultured in preference to white, but great care was taken not to culture any part of the brain that was in close contact with meninges, in order to prevent the growth of fibroblasts. It was found that older embryos gave the most profuse cultures of microglia, a fact that coincides with Rio-Hortega's observation that microglia do not appear until the last days of fetal life.

The striking feature of microglia in culture is the variability in the form and structure of these cells. This is the result of the activity of the microglia in its phagocytosing and motile function. The various forms found in cultures correspond to those described by Rio Hortega. The form and structure of the microglia will depend on the age of the culture. During the first twenty-four hours, there is no change in the original piece of tissue cultured. After a varying length of time, there appear in the culture a number of small dark flecks which increase in time, and which are identified a little later as round cells the protoplasm of which contains numerous small granules. These granular elements represent the embryonic microglia in the cultures. At the end of forty-eight hours there is a large number of microglial elements at the edge of the cultured tissue. These cells are spherical, with a round nucleus that is often eccentric, and with a protoplasm of varying size which is filled with granules and often contains vacuoles. An interesting feature of the embryonic microglial forms consists in the presence of fine, threadlike, pseudopodic prolongations similar to those seen in cultivated monocytes, resembling cilia and engaging in slow, irregular movements. These cilioid forms lose and regain cilia and are constantly changing form. The cilia formation is entirely independent of the pseudopod formation of the microglia. Costero assumes that these cilia are present in vivo, but that the action of formaldehyde and other fixatives so injures them that they cannot be demonstrated. At the periphery of the culture there appear rod cells. From these it is a short step to the free polymorphous cell, and finally to the starlike forms with branching, active pseudopodia. The new polymorphous cells remain unchanged in structure in comparison to the rod cells; i. e., they contain the hyaline protoplasm and transparent nucleus. For a short period some of these elements anastomose. Many of the forms of this period correspond exactly with the pseudopodic and ameboid forms described by Rio Hortega in pathologic processes and in injuries to the brain. Finally, the cultured microglia reaches a form that is comparable to that

seen in the normal tissue of the human being. These adult forms have not been seen as frequently as the less mature elements, chiefly because of the nature of the medium, which differs chemically from normal tissue and which is less dense than the network of the normal brain. Gitter cells appear as a regressive phenomenon in the cultures. They are identical with the gitter cells described by so many investigators.

Microglia in culture possesses a very marked activity. In the early hours of the culture the activity is carried on by the cilia, which are in constant motion. Later these cilia disappear and are taken up by the exoplasm. At a later stage pseudopodia appear. These are less numerous than the cilioid bodies, and their activity is not so great. The speed of movement of microglia in cultures varies a great deal, and depends on the stage of development of the cells and the nature of the medium. Early after the culture is made, movement is very slow. Later, the movement of the microglia is more rapid. Their most rapid movement is observed in cells that penetrate beyond the edge of the culture. The speed of movement of the microglia is aided materially by the presence of fibroblasts in the culture, by means of which the microglia can attach their pseudopodia to something and travel much faster. One of the most striking features of microglia in culture is stereotropism, the tendency to group themselves around any object with which they come in contact. If one throws a small bit of wool or some other lifeless particle into the culture, it is surrounded by microglia. This ability to attach itself to the surface of objects in culture explains the frequency with which microglia is in contact with ganglion cells and blood vessels in nerve tissue. The phagocytic action of microglia is shown with absolute clearness in cultures. All sorts of bodies, especially red cells, are phagocytosed. Leukocytes are phagocytosed by the microglia in culture. Foreign bodies, such as pieces of paraffin, are quickly surrounded by microglia, and then phagocytosed. The phagocytic action of microglia is particularly apparent when the culture is infected. The microglia cells take up the bacteria readily. In fact, they have such an affinity for them that the smallest colony of bacteria is readily detected by the huge accumulation of microglia around it. The cells ingest carmine granules. Mitotic figures are extremely rare in cultures of microglia, just as they are in the human being in vivo. Costero points out that the rod-cell forms of microglia found in culture are wandering forms, whereas the phagocytic forms are resting.

Costero states that the microglia is a cell that is mesenchymal in origin, and has nothing to do with the neuroglial elements that remain inactive in cultures. This view had been originally propounded by Rio Hortega.

ALPERS, Philadelphia.

NEUROLOGIC SEQUELAE OF EPIDEMIC ENCEPHALITIS. M. RISER and PAUL MÉRIEL, Rev. d'oto-neuro-opht. **9**:323 (May) 1931. (Continued from April.)

Some of the disturbances of the great organic functions existing during the acute stage may be prolonged into the chronic stage. Among the respiratory troubles are spasmodic polypnea, occurring toward night and sometimes alternating with bradypnea, spasmodic cough, hiccup, respiratory tics and abnormal rhinolaryngologic sensations, which often confuse the diagnosis. Many of the disturbances are of dystonic origin. Thermic and circulatory disturbances, represented by an inversion of the thermic rhythm, terminal hyperthermia, tachycardia, bradycardia and hypotension, are often associated with respiratory difficulties. Camus and Roussy have shown that the neuro-endocrine disturbances, such as obesity, diabetes insipidus and glycosuric and adiposogenital syndromes, with the existence of a normal hypophysis, are caused by involvement of the infundibulotuberian region by the encephalitic process. Insomnia lasting for long periods, which is well borne, or hypersomnia is sometimes present.

Mental disturbances at times precede the neurologic signs. In adults, depressive syndromes with egocentrism and bradypsychia predominate. Dementia is rare. In

adolescent children, symptoms of psychomotor excitation, anger, irritability, liberation of perverse instincts and hysterical manifestations are the rule. In the series reported there were 68 patients, aged from 11 to 20 years, of whom 20 had mental disturbances, in no case unmixed with neurologic signs. Twenty-two of the patients had purely psychic manifestations over a period of several months and then the first signs of parkinsonism appeared.

The cerebrospinal fluid shows nothing characteristic. Bériel and Fribourg-Blanc maintained that a content of dextrose exceeding from 0.5 to 0.6 Gm. per liter was abnormal. The authors examined 70 patients and only eleven times found a content of more than 0.7 Gm. They also examined the fluid in 2,000 instances in normal persons and those suffering with other diseases, and found 0.7 Gm. frequently and, rarely, even as much as 0.8 or 0.85 Gm.

None of the syndromes enumerated is pathognomonic for epidemic encephalitis. In many cases a retrospective diagnosis of encephalitis is impossible, even from the pathologico-anatomic observations. The cases may be divided into four groups: (1) The acute phase has been characteristic, followed by a free interval of from six months to ten years, and then one or more of the dystonias appears. In such cases the diagnosis presents no difficulties. (2) The clinical picture of the acute stage is less characteristic, consisting only of fever, somnolence and diplopia. If syphilis can be eliminated, the diagnosis is clear. (3) The invasion has been manifested by backache, headache and a mild angina, and the condition has been labeled "grip." In such cases such flimsy evidence does not warrant the diagnosis, except in those instances in which exposure to the contagion of epidemic encephalitis is plain. Two sisters, seen by the authors in 1925, exemplify this. One had a typical attack of acute epidemic encephalitis; at the same time, the other had symptoms that were absolutely atypical, consisting only of slight fever, mild redness of the throat and moderate headache and backache, lasting three days. Both patients appeared in 1929 with distinct progressive parkinsonism. (4) In this group the past history fails to reveal even the classic "grip." The patient becomes infected, but the virus remains latent until the dystonias appear.

In the last two groups the diagnosis must be made by exclusion. Congenital affections, choreo-athetosis of Vogt, the dystonias of Little, chronic hereditary chorea, traumatism of the new-born, the chemical intoxications, tumors, dementia praecox, labyrinthine and cerebellar diseases and syphilis are to be eliminated before epidemic encephalitis can be thought of. A slowly progressive parkinsonism in a child or adult, not preceded by a clearly defined acute epidemic encephalitis, in which the above named diseases can be eliminated, constitutes "an excellent stigma of epidemic encephalitis." In young subjects with isolated dystonias that are not congenital, syphilitic, traumatic or due to tumor, the etiologic diagnosis of epidemic encephalitis is justifiable if signs of parkinsonism are present. If the signs are not present, some other etiology must be sought; this applies especially to torticollis.

The fact that there are hiatuses in knowledge of the extrapyramidal syndrome and of the pathologic anatomy, especially with regard to the central nuclei, should be borne in mind. Destructions of the striatum and pallidum in man may not be followed by extrapyramidal signs. "The pathologic anatomy of prolonged epidemic encephalitis (or better, parkinsonism) shows constant, diffuse lesions that are not closely systematized, either qualitatively or quantitatively. However, their mesocephalic predominance and, in particular, the involvement of the locus niger and the striatum are scarcely doubtful. With Bériel, one must distinguish 'a double pathologic movement: one, exudative of the usual inflammatory type, which corresponds to the acute clinical episodes, febrile or not, initial or not; the other is of long duration, degenerative and, like all processes of this order affecting the nerve centers, it has an ineluctable progressive character.'"

The following facts seem to be established: "(*a*) The presence of inflammatory lesions which seem active a long time after the acute period in parkinsonians, which perhaps testify to the presence of the virus in the nerve centers; (*b*) The absence of specific lesions, properly speaking; however, it is necessary to consider as very

important the elective "essential" degeneration of ganglion cells without any other local lesion; (*c*) The absence of specific localization of the lesions for a given syndrome: a precise damage of this or that part of the neuraxis does not correspond to a spasmodic torticollis, a parkinson disease etc., at least, in the present state of our knowledge."

A long critical discussion of the nosographic relations of epidemic encephalitis and optic neuromyelitis, vaccinal encephalitis, Sydenham's chorea, acute ataxia of Leyden, infectious polyneuritis, acute disseminated myelitis, poliomyelitis and multiple sclerosis is summed up as follows: "Modern investigations, especially since the last ten years, put in evidence the existence of acute neuraxites, infectious and caused by unknown germs, neurotropic ectodermoses of Levaditi. They occur in small epidemics or sporadically. Their clinical morphology is extreme and there is no cerebral district which cannot be attacked. The pathologic anatomy, the clinical picture, the study of the ultimate evolution permit us in many cases to classify them as poliomyelitis, multiple sclerosis, neuropticomyelitis, epidemic encephalitis etc. But often the distinction is impossible. Besides, it is more than probable that the neurotropic affections already known are not solely the causes. It is impossible to attribute systematically to epidemic encephalitis all the neuraxites that do not fit in the well determined frames enumerated above. Guillain has emphasized the dangers of such a conception; with him and with Pette, Flateau, van Bogaert, van Gehuchten, Margulis and others, it is necessary to agree that it is still too soon, in the absence of a clear etiology, to disturb too much the group of nonsyphilitic, acute neurotropic neuraxites; etiologic research must come to the foreground."

DENNIS, Colorado Springs, Colo.

TUMOURS INVOLVING THE CAUDA EQUINA: A REVIEW OF THEIR CLINICAL FEATURES AND DIFFERENTIAL DIAGNOSIS. I. M. ALLEN, J. Neurol. & Psychopath. **11**:111 (Oct.) 1930.

A survey of the material available in the literature and in the case histories that the author uses at once draws attention to the fact that it is only in the late and hopeless cases of tumors of the cauda equina that the classic clinical picture is found. The early recognition and localization of these tumors is of paramount importance for successful removal. Although the incidence of these tumors is difficult to ascertain accurately, it would seem that approximately 10 per cent of spinal cord tumors affect the cauda equina.

The classification of Roussy and Lhermitte is fully discussed and considered for the diagnosis of the cases presented, but it is found that usually the clinical picture does not depend on the localization, extent and nature of the tumor. The only conclusion possible is that, in a case in which all of the symptoms and signs are carefully considered, those representing the highest level probably give an indication of the upper extent of the tumor. Otherwise, the tumors appear to involve certain nerve roots, leaving others unaffected. There is, therefore, an interference with some functions while others are quite normal according to no obvious rule.

The localization of these tumors, then, is often extremely difficult. The perpendicular course of the caudal roots within the spinal canal is the chief source of difficulty, for it is possible for a root to be involved in any position from its emergence from the spinal cord to its exit from the spinal canal. Hence, from the signs of involvement of individual nerve roots it is usually impossible to determine the lower limit of the tumor. The lateral position of the tumor frequently can be assumed from the more or less unilateral symptoms and physical signs, while the anteroposterior extension can be recognized from the preponderance of either motor or sensory symptoms.

The following clinical features, when considered together, may give helpful information: (1) pain in the back; (2) segmental distribution of pain in the lower limbs; (3) the upper limit of change in sensation; (4) the level to which the reflexes are involved; (5) the level to which motor functions are affected and (6) the results of lumbar puncture. In other words, the individual case must be con-

sidered carefully on its merits; it is only by so doing and by applying the results of past experience that some idea may be gained of the position, nature and extent of the tumor.

The collected material shows that the application of the general ideas obtained either by a study of the anatomic and physiologic features, or by a comparison of the symptomatology of traumatic lesions of the cauda, will result in a correct diagnosis in most cases only when treatment is no longer of avail. It is essential to separate the symptomatology of tumors of the cauda from that of those due to involvement of the conus, and in order to do this caudal tumors must be defined. They may be considered to be neoplasms localized entirely below the lower border of the second lumbar vertebra. The significance of the disturbance of the sphincters is at once evident, for late and gradual appearance of disturbance then becomes apparent as a feature of caudal tumors, whereas a rapid appearance at any early stage or at any time during the clinical course would appear to indicate that a caudal tumor has become complicated by involvement of the conus.

Pain is the initial symptom in over 90 per cent of cases. In the remaining 10 per cent it appears in a comparatively early stage in the clinical course. In more than three fourths of the cases it appears first in the back, either in the lumbar or sacral region. In only 10 per cent is it ever of a root type in a lower extremity. In spite of the fact that pain is so common, it cannot be used to localize a tumor accurately. The pain in the back is usually a dull ache which increases a little on movement. In other cases it is severe, having a jarring, crushing character. Frequently it is a constant dull ache in the back and affected limb with acute exacerbations which the patient finds almost unbearable. Percussion of the spine, jarring of the head, stepping too firmly on the floor, movements, coughing, straining, swallowing, etc., may aggravate the pain. It is usually aggravated in the recumbent position and relieved in the erect posture. Another point of importance is the frequency of intermissions in the pain before the appearance of physical signs on which a positive diagnosis on clinical evidence alone may be made. One case showed an interval of seven years.

Because of the variability of the roots involved, definite signs and symptoms are not absolute and lumbar puncture appears to be rather important for decision. The author makes a plea that every case of persistent pain in the back, in the sacral region or even part of a segmental area, should have the benefit of spinal fluid investigation. Repeated dry taps are important for often these tumors are gigantic in size and occupy all or most of the spinal canal at that level. Occasionally the discovery of fluid one or two spaces above the site of the dry lumbar puncture is of value in fixing the upper level of the tumor. The lower limit of the neoplasm can sometimes be determined by lumbar punctures or by the introduction of iodized poppy seed oil of low specific gravity and roentgen examination. The characteristics of the spinal fluid obtained below the lesion vary considerably, but in only 13 per cent of the cases recorded was it found to be normal.

In other words, the differential diagnosis of caudal tumors depends on a careful and detailed investigation of the case. Occasionally, sources of difficulty arise, as in the not uncommon association of hypertrophic arthritis of the spine or of spina bifida occulta with the lesions under consideration. In such cases the chances of confusion are lessened by assuming that the clinical picture is a result of the more serious condition until this is proved or disproved. The delay in investigation and the postponement of treatment until a clearcut type of clinical picture is present means in most cases waiting until the condition is beyond the resources of treatment.

BECK, Buffalo.

IV. THE METHOD OF ACTION OF PITUITRIN INTRODUCED INTO THE VENTRICLE. HARVEY CUSHING, Proc. Nat. Acad. Sc. **17**:239 (May) 1931.

The question arises whether solution of pituitary acts peripherally after resorption into the blood stream or directly on the subependymal and thalamencephalic nerve centers. It might be assumed that the substances, after injection into the

lateral ventricle, become resorbed into the blood stream either through the ependyma or the choroid plexuses. This is not probable, at least in the case of solution of pituitary, because when it is given intramuscularly or injected into the blood stream its effect is wholly different from that which follows its introduction into the ventricle. In trying to answer the question as to how the drug acts, Cushing expressed the belief that the negative responses obtained in its administration might give valuable information. These negative responses occur: (1) with insufficient dosage; (2) when the ventricles have been greatly expanded by hydrocephalus, and (3) when the interbrain has been the seat of a tumor. The negative responses in cases of marked hydrocephalus which balloon the walls of the third ventricle and in cases of involvement of the ventricular walls by tumor serve to throw out of action the hypothalamic nuclei, the stimulation of which is assumed to call forth the typical reaction.

V. The Counteractive Effect of Tribromethanol (Avertin) on the Stimulatory Response to Pituitrin Injected in the Ventricle. Harvey Cushing, Proc. Nat. Acad. Sc. **17**:248 (May) 1931.

In this paper, the fifth contribution of Cushing on the effect of injection of solution of pituitary into the ventricle, an attempt is made to determine further the action of this substance and of pilocarpine on the brain stem. In a previous study it was found that in tumors of the interbrain no response is obtained by the injection of solution of pituitary or pilocarpine. This argument is used, therefore, in favor of the view that these substances act on the hypothalamic nuclei. In order to test this hypothesis further Cushing sought for a narcotic inhibiting the thalamencephalic centers and for this purpose used tribromethanol which, like dial-Ciba, acts on the subcortical centers. The drug produces deep, apparently natural sleep, pupillary contraction and fall in blood pressure. If these are essential in origin, the sleep is assumed to be due to stimulation of the sleep center. Tribromethanol is antidotal. Two patients were observed, in each of whom there was a typical reaction to solution of pituitary injected into the ventricle while there was no reaction with the patient under tribromethanol. It was therefore concluded that tribromethanol "presumably causes its effects by action on centers of the diencephalon, and serves to counteract the stimulatory responses to pituitrin injected into the ventricles."

VI. Concerning a Possible "Parasympathetic Center" in the Diencephalon. Harvey Cushing, Proc. Nat. Acad. Sc. **17**:253 (May) 1931.

The conclusions reached by Cushing in this series of investigations may be summed up as follows: *A*. The active principle of the neurohypophysis is excreted in part into the blood stream and in part into the cerebrospinal fluid. The hormone when experimentally introduced into the blood stream causes pallor from vasoconstriction and stimulates the musculature of the lower bowel; when introduced into the ventricle, on the contrary, it causes flushing, sweating, salivation, lacrimation, vomiting and a pronounced fall in body temperature. The former reaction bears resemblance to a sympathetic discharge combined with a sacro-autonomic effect; the latter appears to be essentially a cranial autonomic or parasympathetic effect. Pilocarpine introduced into the ventricle gives a highly similar response.

These responses to intraventricular injections of solution of pituitary and pilocarpine are counteracted by atropine, whether given subcutaneously or intraventricularly; they, moreover, appear to be abolished when the tuberal portion of the interbrain is highly distended by hydrocephalus or is the seat of a tumor, and their action, furthermore, is checked by tribromethanol, a narcotic that presumably acts chiefly on the interbrain.

B. A rich arborization of unmyelinated nerve fibers is known to pass from the tuberal nerve centers to ramify in the neurohypophysis. The posterior pituitary hormone or a substance indistinguishable from it has been shown to be increased in the cerebrospinal fluid after electrical stimulation of the tuber. It has also

been shown to be increased in amount in the fluid in animals under emotional excitement. The interbrain has been shown to be the seat of the primitive emotions that are released from their cortical inhibitions by experimentally disconnecting the nerve paths from the frontal cortex. Theoretically, animals so decorticated should show an increase of posterior pituitary hormone in the cerebrospinal fluid.

C. As a working concept it may be assumed: (1) that under emotional stimuli the posterior pituitary hormone becomes discharged through its specific and histologically demonstrable thalamencephalo-hypophyseal mechanism; (*2*) that the active principle or a portion of it enters the cerebrospinal fluid, whence, presumably by diffusion through the ependyma, it may come to act on thalamencephalic nuclei from the parasympathetic apparatus, and (3) that conditions may conceivably arise in which posterior pituitary hormone is discharged into the fluid in sufficient strength to call forth a parasympathetic (cranial autonomic) response as diffuse in its character as is the response on the part of the sympathetic system brought about by the discharge of epinephrine. The neurohypophysis, in short, may conceivably bear a somewhat similar relation to the parasympathetic division as the suprarenal medulla bears to the sympathetic division of the autonomic nervous system.

ALPERS, Philadelphia.

CERTAIN PATHOLOGIC CONDITIONS ABOUT THE CHIASM, WITH SPECIAL REFERENCE TO PITUITARY ADENOMAS. T. B. HOLLOWAY, Arch. Ophth. **6**:81 (July) 1931.

Ophthalmologists have been unusually fortunate recently in that the literature has included much work and many detailed observations and discussions on the signs and symptoms of pathologic conditions about the chiasm. This article continues the same study from another standpoint, though it is based largely on observations due to pituitary adenomas. The author's discussion of the mechanism of papilledema is of interest. He acknowledges the mechanical side of this condition, but also calls special attention to the part each normal structure plays and their anomalies and relationships, both normal and abnormal, in the development of papilledema.

The review of the symptomatology is based on thirty-one selected and verified cases of pituitary adenoma. In this group, the two earliest and consistently outstanding symptoms are headache and failing vision. Lacrimation and photophobia were also noted. In most of the cases the headache was frontal. The average age was 34. The outstanding ophthalmologic symptom was optic nerve atrophy, which was present in 77.4 per cent of the cases. In 6.5 per cent of the cases, there was early choking. In 16.1 per cent, the patients had normal disks associated with impaired vision. Among the twenty-four cases showing atrophy, there was a yellowish tint in ten, or 41.6 per cent, while a waxy appearance, with or without a yellowish color, was observed in seven instances, or 29.1 per cent.

The fields of vision are discussed in great detail. The defects usually appeared as an indentation in the superior temporal quadrant of each field, proceeding downward into the temporal fields and then upward into the nasal fields. It was the author's experience that, in the majority of patients showing the terminal defects of this condition, the greater part or all of the remaining or residual field was in the superior nasal quadrant. Bitemporal hemianopia was present in 54.8 per cent. In two cases, there was a temporal loss of vision in one eye, while the other eye was normal; in two cases there was temporal loss of vision in one eye while the other eye was blind. In 16.1 per cent of the cases, there was homonymous hemianopia. In one case, a superior altitudinal hemianopia was present, and in another, an inferior altitudinal hemianopia was found. Two patients had concentric contractions of the fields. In one instance only was there a marked temporal defect in the color fields alone. Well defined circumscribed scotomas were present in five instances, or 16.1 per cent.

In discussing the oculomotor nerves, a history of diplopia was elicited in three patients. One case showed involvement of the third nerve, and another of the

sixth nerve. Nystagmus was observed only once, and exophthalmos was not observed at any time.

Throughout the entire article, the author compares his observations with those of others. His conclusions are: In cases of adenoma, depreciation of vision is usually the first symptom noted; it is sometimes preceded by headache, usually early in the disease. The most frequent manifestation of the disk is a primary optic atrophy (in 84.7 per cent), and this is observed about ten times as frequently as is choked disk. The atrophy assumes a yellowish tint in about 42 per cent of the cases. In about 29 per cent, the disk may present a waxy appearance. The hemianopia produced tends to be irregular rather than having a vertical line that sharply differentiates the obliterated from the remaining field. A bitemporal hemianopia (74.8 per cent) occurs about seven times as frequently as a homonymous defect. Concentric contraction and altitudinal defects occur in about 2 per cent of the cases. Involvement of the extra-ocular muscles is at times noted, and it is possible, as has been suggested by Beckman and Kubie, that diplopia may occur independently of any pure muscular palsy.

SPAETH, Philadelphia.

PSYCHIATRY AND ABNORMAL PSYCHOLOGY. ARTHUR ERNEST DAVIES, Brit. J. M. Psychol. **10**:312 (Jan.) 1931.

While psychiatry is as ancient as medicine, modern psychiatry has evolved out of medical specialization and has included within its scope phenomena that have been discarded by other specialists. The study of these phenomena has shown that successful treatment of mental disorders demands knowledge and skill not possessed by the general physician. The author uses the term psychiatry in its strict medical sense: namely, the diagnosis and treatment of derangement of behavior with a view to classification. This tendency to create entities that are as well defined as in other and older branches of medicine has given confidence, but it has been misleading. Two types of psychiatrists are described: one group seeking only a neurologic lesion, the other seeking in addition to find mental lesions. Both of these approaches are included under the name of psychiatry. Neurologic psychiatrists start with the assumption of the physical nature of behavior disorders. He studies the traits according to the established principles of other branches of medicine because he argues that since psychiatry is a branch of medicine, it must be governed by the same principles. The inherent weakness of the neurologic, or the strictly medical, point of view, is that it cannot conceive that a mental disorder has any but a physical basis. Psychologic psychiatrists do not deny that behavior disturbances are conditioned by neurologic lesions; however, they carry to the study and diagnosis of these conditions a point of view that goes beyond the nerve lesion and deals with mental phenomena. These are phenomena which the neurologic psychiatrists place outside the realm of scientific investigation, and hence the psychologic psychiatrist is regarded as unscientific.

The author then discusses the basis for the scientific approach, and quotes Hart as describing science as "the term applied to a systematic set of beliefs which have been reached by the application to the object of a particular method, the method that has established physics and chemistry." He shows that when psychologic sciences follow these methods, their results will become as much a part of scientific medicine as are the contributions of neurologic psychiatrists. He points out the need of a well ordered mental pathology that would "compare favorably in extent and thoroughness with that which has placed neurologic psychiatry in its relatively secure position." He shows that the psychologic psychiatrist is in a sounder position from a scientific standpoint because he is not bound down to a consideration of one set of facts, as is the neurologic psychiatrist. He has a broader base on which to build his science and can go beyond the boundaries of the physical sciences to seek the facts that cause the sickness of the mental patient. This leads the author to conclude that modern psychiatry should be regarded as a branch of science and not as merely a branch of medicine.

The psychologic psychiatrist works at a greater disadvantage than the neurologic psychiatrist because of the lack of an organized technic. Attempts to make up

for this lack have "eventuated in theories of mental disease which, for the most part, have no foundation in a systematic knowledge of normal mental life and which are little more than generalizations that are expressive of the physician's personality rather than of a scientific analysis of the symptoms of the disease." A physician, as a rule, is not oriented in normal psychology. This has led to the building of theories regarding the nature of mental life from the rather intensive observations that have been made on sick people. G. Stanley Hall is quoted as warning that psychoanalysts will be "somewhat too ready to apply their findings to the operations of the normal mind." He implies that the psychoanalytic school of today has not heeded this warning. The author thinks that psychologists must be allowed to work hand in hand with the medical specialists if a more orderly and scientifically established mental pathology is to be built up.

ALLEN, Philadelphia.

PICK'S DISEASE IN BROTHERS. E. GRÜNTHAL, Ztschr. f. d. ges. Neurol. u. Psychiat. **129**:350, 1930.

The occurrence of Pick's disease in two brothers offers some data in the explanation of the etiology of this disease. The view of Gans that the disease represents a heredodegeneration has not been widely accepted, though a few cases have been reported in sisters and even in a family.

The disease in the two brothers reported by Grünthal ran a very similar clinical course, the duration of the illness being five and one-half and two and three-fourths years, respectively. The clinical course could be divided roughly into three stages: (1) a certain loss of inhibitory powers, a restlessness and a labile emotional tone; (2) disturbances in higher functions, such as memory and understanding, and the appearance of motor phenomena; (3) complete mental dulness, often with contractions of the extremities.

Macroscopically, the brains of the two brothers showed rather extensive atrophy. In one case, with a duration of five and one-half years, there were: atrophy of basal portions of the frontal lobe, the temporal pole and the inferior portion of the right insula; a flattening out of the caudate nuclei, and an increase in color of the pallidum; a slight atrophy of the second and third convolutions of the right temporal lobe and of the hippocampus. In the other case the atrophy involved the basilar portion of the left frontal lobe, the left temporal pole, the basilar portions of the cerebrum, the right temporal convolutions and the gyrus hippocampi. The basal ganglia were implicated as in the first case.

Microscopically, glial studies showed a profuse glial proliferation in the areas of greatest atrophy, such as the orbital surface of the frontal lobe and the temporal pole. The callosum was rich in glia fibers. In the second case, the entire frontal lobe was richly invaded by glia fibers, particularly the orbital surfaces, the region of the insula, the callosum and also the temporal pole. The cortex of the orbital gyri showed almost a complete loss of architecture in the layers below the external granular layer. There were a marked loss of ganglion cells and a loss of definite lamellation. In the temporal lobe a similar state of affairs prevailed, with a marked loss of cells in lamina III. The cell loss was less marked in the temporal poles. The cornu ammonis showed an increase in glia fibers and astrocytes, and an outfall of Sommer's sector. At the base of the brain there was an increase of glia fibers in the medioventral nucleus of the thalamus, the substantia nigra and the external geniculate body. All these areas were shrunken. Differentiation between caudate and putamen was no longer possible. Around the ventricle were areas of nuclear and fiber hyperplasia. The pallidum showed an abnormal richness of pigment and glia. The substantia innominata showed an increase in glia, and shrinkage spaces around the vessels.

A comparison of the two brains showed a striking similarity between them in the type and localization of the process. The only difference was that in one case the right hemisphere was more involved, and in the other the left. In most cases thus far reported the left hemisphere has been most involved. Grünthal thinks that certain conclusions about the development of the disease can be drawn

from these cases. In the early stages the areas of predilection are the orbital surface of the frontal lobe, the adjacent insula, the temporal pole, the region of the cornu ammonis, the caudate nucleus, the medial thalamus and the substantia nigra. It is worthy of note that the basal portions of the brain are much more implicated than the cortex in the early stages. The white matter atrophies early. The convexity and pallidum are secondarily atrophied. These characteristics are true of the early stages of Pick's disease. Grünthal's patients were young (42 and 45) and died early in the disease. He thinks that in these cases, at least, a hereditary background must be postulated.

ALPERS, Philadelphia.

SOFTENING OF THE TEMPORAL LOBE WITH THE CLINICAL PICTURE OF PSEUDOTUMOR CEREBRI. OTTO MARBURG, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **33**:1 (Feb.) 1931.

A married man, aged 41, two months before admission, began to have attacks of migrainous pains in the left side of the head, with nausea and occasional vomiting. The attacks appeared at various intervals and would last for several hours, during which he would have a sensation of numbness in the right hand. On examination he showed: percussion tenderness over the right side of the skull, slight hypesthesia over the right half of the tongue, very slight paresis of the right upper extremity, with diminution of all forms of sensibility in that limb, and hyperactive tendon reflexes in the right upper and lower extremities. The most important observation was that of astereognosis in the right hand and disturbances in the sense of position of the fingers (right). There was no apraxia, alexia or aphasia. The diagnosis of a focal lesion in the left parietal lobe, perhaps of an early tumor, was made. The fundi were normal. The patient was subjected to radiotherapy, but his condition became worse. Reexamination three and a half months after the onset of the illness revealed some difficulty in understanding spoken words, as well as in finding the proper words, some slurring of speech and paraphasia. There was neither alexia nor agraphia. The sensory disturbances were more marked, especially in the ulnar distribution of the fourth and fifth fingers. There was definite evidence of involvement of the pyramidal tract on the right side and of hyperemia of both nerve heads. All symptoms and signs of an expanding lesion in the left parietotemporal lobe became more manifest, and four months after the onset of the illness, the brain was explored by Professor Eiselsberg. No tumor was found. Following the operation the headache disappeared, but the other neurologic signs remained stationary. Before further neurologic observations could be carried out the patient contracted grippe and within a few days died of pneumonia.

Examination of the brain revealed two pathologic processes: (1) a meningoencephalitis which, in view of the appearance and distribution of the infiltrates in the walls of the blood vessels, is regarded by Marburg as secondary to the grippe pneumonia; (2) the principal lesion which was a softening in the region of the brain supplied by the posterior branches of the middle cerebral artery. In the absence of evidences of syphilis or of metallic or toxic poisoning it is difficult to explain the malacia, which was apparently due to severe changes in the blood vessels, which were remarkable because they did not involve the entire vessel but only its smaller branches, giving rise to multiple, though relatively small, foci of softening. These foci were of two varieties, one of which was far advanced and had already undergone sclerotization and even cyst formation (putamen). The second variety of softenings contained large numbers of fatty granular cells, and some of them had invaded the depths of the temporoparietal lobes and were surrounded by areas of edema, while others were limited to the surface of the brain with destruction of the cortical gray matter. The vascular changes in general were not as marked on the right side of the brain as on the left, but even there one could see early evidences of a status disintegrationis. In view of the fact, however, that vascular changes were found also in areas of the brain in which there were as yet no evidences of parenchymatous involvement, Marburg believes

that the primary basis for the pathologic process was a disease of the blood vessels. He attributes the clinical picture of increased intracranial pressure to the fact that the lesions involved the white substance, because in his experience whenever hemorrhage or softening produces extensive destruction of the white matter, one may expect evidences of increased intracranial pressure.

KESCHNER, New York.

RETAINED PUPILLARY REACTIONS WITH NO PERCEPTION OF LIGHT. S. R. GIFFORD and L. L. MAYER, Arch. Ophth. **6**:70 (July) 1931.

The study of the pupillary reflexes is of great interest to the neurologist. As the author states, the persistence of the direct pupillary reflexes brings up the question whether or not the reaction to light is mediated by a different mechanism from that transmitting the sensation of vision. The usual teaching is that if the pupil reacts to the light stimulus, the patient should be able at least to see light, whether the fundus is abnormal or not. Spaeth's recent article on the pupillary reflexes is discussed, and a study by Janet and McAuley is quoted as follows: The iris reflexes are absent in true blindness (McAuley) except: (*a*) in a lesion high up in the optic pathways above the fibers of the reflex arc to the center for pupillary movement; (*b*) in bilateral lesions of the occipital cortex; (*c*) in temporary retainment in uremia with amaurosis; (*d*) in blindness from certain diseases of the optic nerve in which it seems that the pupillary fibers for the light reflex were more resistant than the visual fibers, and (*e*) in that reaction described by Leber with certain forms of retinal degeneration wherein a slow reaction to light remains even with total absence of light perception.

Many men have spent considerable time on efforts to determine whether there is a pathway outside the retina by which the pupillomotor reactions are carried. Mention of them here is sufficient: Bodenheimer and Korbsch, von Graefe, Magnus, Wirth, Parson, Alexander, Axenfeld, Reichardt, Dunn, Abelsdorff, and especially Hess and Behr and later Hess with Groethuysen. It is almost as interesting that some of these investigators worked on the reverse of the problem, that is, the absence of the direct iris reflex in the presence of light perception. Naturally, the author does not include any of those common cases (either in his article or in a summary of the work of other investigators) or cases in which fixed pupils are present with retained vision from a lesion in the reflex arc, these having no bearing on the problem.

As was pointed out by Hess and Behr, the presence of the direct reflex in the absence of the perception of light cannot be based on a response from the iris itself. The author illustrates this by one of the cases he has studied and reported. This single statement alone is of importance. One case, that of Reichardt, was studied at autopsy. An often repeated controversy arose from this, in that, while the eye was blind certain undegenerated nerve fibers were found in the microscopic sections. It was Magitôt's belief that these fibers were capable of mediating the light reflex, but not the sensation of the visual reflex, namely, visual light perception. Leri, however, has shown that relatively few fibers are necessary to allow the perception of light stimuli. Hess held an opinion against this theory of separate nerve fibers for the two functions. Subsequent to Hess' work, his theory was modified in that there was a suggested separation of the sensory and motor fibers in the external geniculate body instead of in the chiasm as had previously been held.

The authors in summarizing the article call attention to a marked difference between the functions of the receptor mechanism of the pupillary reaction and that of visual sensation. In their case it seems as if the receptors for the pupillary mechanism in the retina were preserved and intact, while those for vision were lost or without function. While this is of interest, the authors themselves state that in their case and certain others, especially those reported by Behr and Abelsdorff, the lesion was definitely in the nerve; hence these cases require almost the assumption of separate fibers in the nerve, unless one considers that fibers capable of transmitting both kinds of impulse may be so damaged that one or the other function alone is lost.

SPAETH, Philadelphia.

THE NEUROSIS IN THE MIRROR OF TIME. WALTER SCHINDLER, Fortschr. d. Med. **49**:431 (May 29) 1931.

Whenever there has been a conflict between morality and instinct a neurosis has resulted. The Bible gives evidence of much conflict and describes anxiety states of demoniacal origin. Among the Greeks one finds the mental harmony of the times disturbed by a profound pessimism of oriental origin. History does not record enough data about the neuroses of Rome, but undoubtedly a conflict between the morals and instincts must have occurred. As for the Middle Ages, one can scarcely find a more neurotic period in history. Witchcraft, demoniacal possession, monasticism and flagellantism led Fridell to term the Middle Ages the puberty of Europe. The seeking for symbols in everything that characterized this period is so applicable to the understanding of the neuroses. The journeys of the flagellants can be recognized as a form of wholesale sickness, as well as the dancing frenzies of men and women who, during the dances, had epileptiform seizures and visual hallucinations. These dances can now be regarded as typical of the sexual religious neuroses of those days. Powerful mass suggestion, supposedly from the Archangel Michael, was responsible for the hysterical Children's Crusade. As time went on, reason and intellect became more active, and the transition period was marked by disappointment in the old gods and general pessimism. This was followed by mysticism such as that of Eckart, on one hand, with the identification with God, and, on the other hand, the development of personalities uninhibited by morality, such as Julius II, Caesar Borgia and Machiavelli. The Reformation brought a moral regeneration to Europe, but the Thirty Year's War plunged the continent again into a period of superstition and all kinds of neuroses. Puritanism in England produced a return to instinctive repression. The reaction toward freedom was seconded by the development of modern science, but was expressed in the extreme by the neurotic Rousseau whose works border on the paranoic. Extreme sensitivity was expressed in the time of Goethe and Schiller, blossoming forth in the neurotic poetry of the Romantic period. This was followed by the growth of capitalism and the doctrine of work and duty, and once more morality superseded instinct. A return of repression produced hysterical signs such as the arc de cercle, various types of paralysis, blindness, deafness, etc. Today we seldom see such types of hysteria. We live in an epoch of return to freer sexuality but still characterized by anxiety that forms the fundamental effect of present day neurosis and is due to a constriction of life's possibilities. This anxiety the author considers an expression of the castration complex and an accompanying feeling of guilt. The World War and threat of death produced an increase in anxiety. Sexual frigidity and impotence seem to be increasing along with the incapacity for self-abandonment in love. The compulsion neurosis is regarded as one of the modern forms of neurosis in which is seen again the conflict of morality with instinct. Sentimentality is on the increase. Man seems to have lost the ability to put up with himself. The invasion of the capitalistic world is followed by the tottering of marriage as an institution. Every obligation is felt as a burden against which the modern "individualistic" personality struggles in every way, and with these conflicts we find ourselves in a very neurotic world.

HART, Greenwich, Conn.

CYSTIC ARACHNOIDITIS OF THE CEREBELLOPONTILE ANGLE, REVEALED BY BILATERAL COCHLEOVESTIBULAR DISTURBANCES. MONIER-VINARD, RAMADIER and CHAUSSÉ, Rev. d'oto-neuro-opht. **9**:500 (July) 1931.

Since tumors of the eighth nerve from the beginning are almost always manifested by disturbance of its function, the otologist is usually the first to see patients with this condition, and on him rests the responsibility to arrive at an early diagnosis. Too often, unfortunately, this responsibility is evaded by failure to make a systematic labyrinthine examination.

An illustrative example is the case of a man, aged 40, who complained of vertigo and deafness which began six years previous to the consultation with a sudden attack of systematized vertigo (objects turned to the right) and vomiting, lasting all night. Deafness and tinnitus in the left ear followed. These attacks were renewed at intervals of about fifteen days. Various treatments and operations had been undergone, but the deafness and tinnitus grew steadily worse.

An examination revealed: intact drum membranes, bilateral deafness, worse in the left ear, shortened bone conduction, lateralization of sound to the right ear and raising of the lower and depression of the upper tone limit. Caloric vestibular reactions were lost on the left side; there was no spontaneous nystagmus; Romberg's test gave normal results, and there was slight deviation to the left in walking. During a period of three months, several more examinations were made, which revealed an amelioration of the deafness in the right ear and a complaint by the patient of a sense of heaviness in the left temporo-occipital region. When now the right horizontal and vertical canals were tested separately, no reaction was obtained from the vertical canals. (No mention is made of such a test being made on the left side.) Normal reactions from both sides were obtained from the galvanic test, except that they were exaggerated. A neurologic examination revealed hypesthesia and asymmetry of the lower part of the left side of the face, slight alterations of the cerebellar function on the left, slight bilateral papillary edema, normal visual fields and anesthesia of the right cornea.

A diagnosis of tumor in the left cerebellopontile angle was made, and an operation was performed. No tumor was found, but an arachnoidal cyst was evacuated. The patient recovered and one month later the hearing in the right ear was much improved, and the corneal anesthesia had disappeared; but the left ear was still deaf, Eagleton's sign of hypertension (loss of reaction from the vertical canals) persisted on the right side, and the remains of the papillary stasis were present. No mention is made of the vertigo and tinnitus.

Emphasis is laid on the fact that unilateral tumors in the angle often produce symptoms of irritation or paralysis of the opposite acoustic nerve. The ménièriform onset, the long duration and the absence of spontaneous nystagmus are mentioned as possible differential points in favor of arachnoidal cysts as against true tumors in the angle. It is to be regretted that the technic of Jones and Fisher was not employed in the vestibular examination, since they have shown the presence of a characteristic syndrome in cases of angle tumor.

DENNIS, Colorado Springs, Colo.

SOME HISTORICAL PHASES OF MANIC-DEPRESSIVE SYNTHESIS. SMITH ELY JELLIFFE, J. Nerv. & Ment. Dis. **73**:353 (April) 1931.

The author reviews the history and gradual evolution of the manic-depressive conception, beginning with the development under Kraepelin. In the 1889 edition of his work, mania, melancholia and periodic and circular psychoses were described as entities. By the fifth edition of 1896, mania had become the manic form of the "periodic psychoses," while melancholia was conceived of as an anxious depression of the presenium. Later, Kraepelin began to doubt the entity of melancholia as separable from the circular psychoses and believed that certain cases of the manic-depressive psychosis might develop primarily in the presenium. In the eighth edition, the majority of melancholic types in the presenile psychotic groups were transferred to the manic-depressive group. The ninth edition, appearing after Kraepelin's death, contained Lange's new presentation of the kraepelinian system without any fundamental changes. Later additions to the manic-depressive concept came from fields of psychology, and studies in heredity from Kretschmer's body-form correlations and from the psychologic sciences. The author believes that the real advances in understanding are recorded in the sphere of etiology, while the symptomatic picture of the disease loses its importance.

The reader is then conveyed to remotest antiquity in the search for the origin of the concept. Literature abounds with descriptions of the state from Nebuchad-

nezzar to "The Mind That Found Itself." Mania, melancholia and paranoia were more or less synonymous terms with the hippocratic writers. Mood swings, however, were described by Hippocrates, Plato, Asclepiades, Aretaeus, Celsus, Galen, Alexander of Tralle and others. In the works of Aretaeus of Cappadocia, the manic-depressive cycle is specifically delineated, although it is evident that he did not recognize it as a specific disease entity. Lengthy excerpts from the works of Aretaeus are quoted by the author. For a thousand years these concepts of mania and melancholy were repeated, while the demonology of Christianity became rampant. Melancholia became allied to phases of the moon, and red hot irons were used for mania. In the Elizabethan era, Felix Platter, a clinical psychiatrist, and Richard Burton, an erudite student of books, made interesting contributions to the concept. Platter drew up a new systematization of abnormal neural states in which melancholia was described as a form of mental alienation in which the imagination and judgment are perverted, so that the patients become sad and fearful. In his description of cases, schizophrenia, dementia paralytica and organic psychoses can be recognized. Burton's immortal "Anatomy of Melancholy" contains not a morsel of concrete psychiatry amid its ocean of literary abstractions. In the eighteenth century the therapeutic advances made by Pinel are coupled with his useful simplification of preexisting classification, but the conception of the manic-depressive nucleus does not appear until the time of his followers, Falret and Baillarger. In developing the concept of cyclothymia, Falret preceded Kahlbaum by several years, and the disease was termed by him "folia circulaire." Prior to Kraepelin's contribution some useful work had been done by Griesinger and Krafft Ebing.

HART, Greenwich, Conn.

MASTICATOR FACIAL HYDRORRHEA, FORMING PART OF A FACIO-OCCIPITO-SYMPATHETIC SYNDROME. PAUL REBIERRE, Rev. d'oto-neuro-opht. **9**:435 (June) 1931.

Following a gunshot wound (bullet not removed) between the lobule of the right ear and the ascending ramus of the jaw, without lesion of the first and second cervical vertebrae, a man, aged 49, presented the following sequelae: peripheral facial paresis, frequent slight spasm, affecting especially the commissure of the lips, hardness of hearing, tinnitus, slight myosis and facial hydrorrhea. The hydrorrhea was induced by chewing and occupied an area of the temporal region. The patient felt well physically and mentally, and there was no other complaint except a right suboccipital neuralgia at Valleix's point and pain in the posterior hemicranium. The pain was increased by certain lateral movements of the head.

The author has reported a case of partial facial hyperhydrosis, corresponding to a region of sympathetic nerve distribution (*Rev. d'oto-neuro-opht.* **8**:23 [Jan.] 1930).

The present case exhibits, in addition to the hydrorrhea, associated lesions of the peripheral cerebrospinal system. The trauma has produced various symptoms of damage to the facial and suboccipital nerve of Arnold and to the vegetative system. The myosis is a part of the anterior sympathetic syndrome of Claude Bernard-Horner. In the case of Souques, chewing nonsapid substances did not bring on the sweating, while in the present case the ingestion only, without mastication, even of sapid food, was without effect. In the author's former case, neither the chewing nor the ingestion of ordinary food, sapid or nonsapid, caused sweating, but only the ingestion of pork or digestive disturbances caused the condition. There are other exciting causes, for instance, the warmth of the bed.

Most cases of this type are consecutive to lesions of the parotid region, but sometimes this is not true. It is a question whether some cases have not a neuropsychiatric pathogenesis — a possibility of conditioned reflexes based on a morbid habit. The surface affected in the present case is smaller than is usually seen, and corresponds well to the zone of distribution of the auriculotemporal nerve.

Certain posterior headaches in subjects with disorders of the facial mass, especially infections of the nasal sinuses, may be explained by analogy. The patient

showed signs of a paravertebral sympathetic lesion, the posterior sympathetic syndrome of Barré, as well as of a suboccipital neuralgia. The missile straddles the first two vertebrae where the second cervical nerve emerges and anastomoses with branches from the first and third nerves to form the nerve of Arnold, which innervates the posterior cranium. Inflammation of the lymphatic and cellular tissues of this region could easily produce the same results, and such an inflammation might be secondary to anterior infections, instead of, as in the present case, being caused by the projectile. In fact, a large lymph node that received vessels from the nasal mucosa is found near the nerve plexus described. Thus a sinusitis or nasopharyngitis could irritate the suboccipital nerve and so explain certain, if not all, posterior headaches.

DENNIS, Colorado Springs, Colo.

TREATMENT OF TETANUS BY INTRATHECAL INJECTION OF CARBOLIC ACID. S. SUVANSA, Lancet **1**:1075 (May 16) 1931.

As the recognized treatment for tetanus with daily intrathecal injections of from 12,000 to 20,000 units of concentrated antitetanic serum is uncertain and often disappointing in its results, the author was induced to use phenol. This treatment was suggested by the fact that phenol destroys tetanus toxin in vitro. Fresh leukocytes were obtained by lumbar puncture in a case of tetanus in which serum had been administered twenty-four hours previously. (This always produces a mild aseptic meningitis.) Equal units of cerebrospinal fluid and different strengths of the solution of phenol in physiologic solution of sodium chloride were mixed and incubated for an hour. A 1:400 solution of phenol was discovered to be the strongest solution that did not affect the leukocytes. This solution has a specific gravity of 1.006, equal to that of cerebrospinal fluid. Solutions were prepared for treatment by adding 400 cc. of physiologic solution of sodium chloride to 1 cc. of liquefied phenol which had been boiled before use. The most satisfactory dosage appears to be between 30 and 40 cm. in adults, and between 12 and 20 cc. in children, but it must be adjusted according to the severity of the individual case.

Although the number of patients treated is small (fourteen), Suvansa is of the opinion that phenol when given intrathecally is a specific remedy against tetanus. Four patients did not recover, but their conditions were so far advanced that they were either in a state of cardiac or respiratory failure or had a serious complication. The ten patients apparently owe their lives to the treatment, for they had severe cases and were unlikely to recover spontaneously. Some patients received antitetanus serum intravenously, but the amount was not sufficient to effect a cure. A remarkable case of tetanus neonatorum ended in recovery.

There were some complications. An irritation of various cranial and spinal nerves occurred, but these symptoms neither were lasting nor did they cause chronic involvement of the nervous system. A rash, varying in character and intensity, appeared between the first and seventh days. It abated without treatment, for it was due probably to the elimination of the phenol through the skin. Acute nephritis was present in three cases. The treatment, therefore, should not be given to patients evidencing damage to the kidney. The advantages of the phenol therapy are: (1) its action is certain; (2) one injection suffices; (3) the cost is insignificant; (4) the medication is always available. The only disadvantage is the possible danger in chronic disease of the kidney.

BECK, Buffalo.

AMENTIA AND THE CATATONIC SYNDROME. I. F. SLUCHAYEVSKY, Rev. psychiat. neurol. & reflexol. (Leningrad) **5**:49, 1930.

Under the term "confusio mentalis acuta," and later under the term amentia, Meynert described a disease the main feature of which was a disturbance in the field of coordination of perceptions. Outwardly it expresses itself in the feeling of confusion, bewilderment and surprise, with an inability to grasp outside impres-

sions and loss of orientation in time, space or person. Kraepelin looked on amentia as a symptomatic psychosis associated with some definite infection. Amentia may resemble and may be associated with such clinical pictures as are found in schizophrenia or the affective psychoses.

The author presents the history and the clinical pictures of several cases of amentia associated with a definite catatonic syndrome. All the patients were persons between the ages of 20 and 30 who, following an infection such as influenza or typhoid fever, developed a state of confusion with difficulty in thinking, distortion of the outside world, hallucinations and hazy recollections of some of the periods of the illness. These cases also showed symptoms that one usually associates with dementia praecox, such as negativism, mutism, a tendency to assume fixed postures, stereotypy, impulsive behavior, refusal of food and lack of interest in personal appearance. The author believes that acute infections prepare a fertile soil for auto-intoxications. In three cases there were important psychogenic factors that helped to break the resistance of the patients. In the group of five cases, four patients have recovered and one is recovering at the present time. In all cases there was a loss of orientation and hallucinations. The patients acted as if they were in a dream. Besides the physical illness, there was also an exhaustion. With improvement of the mental condition, there was also an improvement in the physical condition with a marked gain in weight. The catatonic syndrome was so prominent that it often obscured the typical features of amentia. The author does not agree with Bleuler, who makes a diagnosis of amentia only after a prolonged observation of the patient does not show any schizophrenic symptoms. Although amentia may be associated with any of the functional psychoses, association with catatonia is usually found in the younger age groups.

KASANIN, Boston.

CONTRIBUTIONS TO THE STUDY OF SUBARACHNOID HEMORRHAGE; A SPECIAL SYMPTOM COMPLEX OF THIS LESION. N. A. POPOW, Arch. f. Psychiat. **92**:304, 1930.

Popow reports seven cases that he has observed, with a review of material reported in the literature. He finds that patients suffering from subarachnoid hemorrhage present a well defined syndrome consisting of a characteristic onset, development and course, clinical picture and cerebrospinal fluid changes. The onset is apoplectiform, with severe headaches of a continuous character which extend throughout the course of the disease. Consciousness may remain clear or show a short lapse. During the development of the disease one usually finds nausea or even vomiting, vertigo, insomnia or drowsiness and irritation phenomena, such as stiffness of the neck and a positive Kernig sign. The degree of intensity of the symptoms is not necessarily parallel with the seriousness of the disease and its progress. In the early stages of the disease some cases present focal signs, such as paralyses and weaknesses. A number of cases described by the author seemed to show a special syndrome in which focal signs, especially paralysis of the sixth nerve and light unilateral weakness of the facial nerve, were particularly prominent. He calls this the "abducens symptom complex."

The early development of all of the symptoms would differentiate subarachnoid hemorrhage from meningitis. A rise of temperature is rare; it does not reach any great height, and there are no chills or herpes. Lumbar puncture shows primarily an admixture of blood with the fluid, the blood remaining of the same intensity throughout the tap. Later, during the process, the fluid may show a yellowish discoloration. Lymphocytosis in the fluid may be either absent or not very high; the mastic and colloidal gold reactions are usually negative. Therapeutically, the author advises repeated lumbar punctures and thinks that good results are obtained in this way. Nothing conclusive can as yet be said about the special etiology and manner of development of the lesion.

MALAMUD, Iowa City, Iowa.

INTRACELLULAR PARASITIC FIGURES IN DISSEMINATED SCLEROSIS. P. GUIRAUD, Encéphale **26**:349 (May) 1931.

This article has its histologic basis in a patient suffering from disseminated sclerosis, a man, aged 34, who nine years before had presented a confusional state with visual hallucinations. This was followed by a kind of delirium and auditory hallucinations. Early in 1930, he presented an intention tremor, adiadokokinesis, incoordination in walking, formication and pains in the lower extremities. A short time later, he showed left hemiparesis, exaggerated reflexes, vertigo and nystagmus. He died in August, 1930, from development of acute myelitis. Section of the central nervous system showed cells with masses of granular bodies containing lipoid droplets. The microglia cells were huge, with much cytoplasm. There were noticeable concentric rings of microglia. The vessels showed intense perivascular infiltration with plasma cells. Innumerable plaques occurred in the cord and bulb, some appearing fibrous and old, but for the most part newer in appearance. The most striking peculiarity was the number of fibrillary neuroglia cells undergoing cytoplasmic hypertrophy. The nuclei were large, eccentric and often multiple. There were numerous granulations in these hypertrophic microglia cells, usually near the periphery, sometimes numbering from three to five in a single cell. Three stages in the development of these intracellular bodies are described: (1) The bodies are small, oval, homogeneous, from 1 to 2 microns in size, with a strongly chromophilic nucleus; (2) the chromophil substance is located at the two poles, with almost no coloration of the intervening substance; the size measures up to 3 microns; (3) the oval is much swollen in the central portion. The author believes that these bodies are exogenous parasites, basing this opinion on their constancy and size, regularity, structure, complexity and chromatic nature. He quotes the work of Steiner, who claims to have found spirochetes in this condition. He believes these parasites to be identical with the "spirochetal débris" of Steiner.

ANDERSON, Los Angeles.

INFLAMMATORY MANIFESTATIONS IN MULTIPLE SCLEROSIS. LE ROY M. A. MAEDER, Arb. a. d. Neurol. Inst. a. d. Wien. Univ. **33**:63 (Feb.) 1931.

Seven cases of multiple sclerosis were examined histopathologically. In six cases the duration of the disease could be ascertained definitely; it varied from six months to eighteen years. In most of the cases the sclerotic foci were free from any infiltrate. In these cases the meninges were also free from infiltrates. However, in areas in which the sclerotic focus was not completely fibrosed, a definite vascular infiltrate was observed. It is also significant that this vascular infiltrate had the same character in the case of eighteen years' duration as in the case of six months' duration. The infiltrate was most marked in the medium-sized and larger veins, was less so in the arteries and was entirely absent in the capillaries. The infiltrate was always found in the vascular wall and never in the parenchyma. The most marked infiltrates were observed in the blood vessels at the margins of the sclerotic foci or near them. In no case, however, was there diffuse vascular infiltration. This was also true of the infiltrates in the vessels of the meninges. The infiltrates consisted of lymphoid cells or of polyblasts, although occasionally plasma cells and very rarely eosinophils, monocytes and macrophages were seen. Leukocytes were very rare. The observations correspond well with those described by Pette in acute multiple sclerosis. The fact that such infiltrates were found only within or near the sclerotic foci is emphasized by Maeder because it shows that they were not due to the general reaction of the nervous system that is usually observed as an expression of a septicopyemic process of the type that all these patients showed during the terminal stages of the disease. From the results of this investigation Maeder believes that Marburg's suggestion that the term multiple sclerosis be discarded and the disease designated as "encephalomyelitis periaxialis scleroticans" should be adopted.

KESCHNER, New York.

RETINAL ARTERIAL TENSION IN CERTAIN CEREBRAL SYNDROMES. CARLOTTI and JACQUET, Rev. d'oto-neuro-opht. **9**:493 (July) 1931.

The authors made a number of observations of retinal arterial tension in four groups of persons, using the sphygmomanometer of Bloch-Verdin, as modified by Bailliart. The average reading in the normal group was: maximum 100, minimum 35. The second group comprised cases of general hypertension with no cerebral conditions but with retinal lesions. In this group the local diastolic pressures averaged almost half as much as the general diastolic pressures. In the third group were patients with cerebral diseases, with or without ocular disorders. In these it seemed "that the cerebral hypertension, indicated by the retinal hypertension, played a rôle in the vertiginous phenomena." The fourth group was represented by one case of cerebral tumor. "In this case the relative retinal hypertension foretold the papillary stasis."

The authors conclude that measurements of retinal arterial tension by the method of Bailliart involve causes of error residing in the instrument itself and its method of use. Errors of technic are due to: (1) pushing the globe laterally at the same time that it is compressed, resulting in loss of force; (2) the use of an assistant in the application of the instrument and the difficulty of exercising uniform pressure; (3) the patient, his emotivity, psychic state and, especially, intracranial hypertension which influence the readings at successive examinations; (4) simultaneous compression of the veins and arteries, which disturbs the return circulation.

"However, the same observer, with the same instrument, can get useful information in certain cerebral troubles from vascular hypertension or perhaps from hypotension, and in certain cases of cerebral tumors before the phase of papillary stasis."

DENNIS, Colorado Springs, Colo.

CRYSTALLIZATION OF HEMOGLOBIN IN VARIOUS AGES OF LIFE. F. NICOLETTI, Arch. di antropol. crim. **50**:386, 1930.

The author studied the morphologic aspect of the crystals of hemoglobin in relationship to age. Hemoglobin crystallizes in the reduced state. The crystallization in fresh venous blood and in coagulated blood takes place more promptly than in desiccated blood. The precipitation of crystals in venous or coagulated blood during intra-uterine life begins within from twelve to fourteen hours, and within from twelve to thirty-four hours during extra-uterine life. In desiccated blood, the respective figures are from twenty to twenty-four, and from twenty to seventy-two hours. Morphologically, the crystals have the same aspect whether they are precipitated from fresh, coagulated or desiccated blood. The paramarginal precipitation of crystals on a preparation is always more prompt and more rich than the central. The hemoglobin of the embryo, of the fetus, of the new-born and of infants during the first two or three weeks of life crystallizes in the shape of needles or of fine sharp-pointed rectangular tablets in a flutelike arrangement. The hemoglobin crystals in persons of more advanced age are precipitated almost exclusively in the shape of flat rectangular tablets of larger size. Such tablets are a more developed (mature) form of crystal. It is on their presence or absence that the differential diagnosis of the age of the person may be based. The study of morphology of the crystals of hemoglobin offers, therefore, an application in medicolegal practice.

YAKOVLEV, Palmer, Mass.

INVESTIGATIONS ON THE PATHOLOGY OF EPENDYMITIS. P. REDAELLI, Riv. di pat. nerv. **36**:455 (Nov.-Dec.) 1930.

The author, using abundant human and experimental material, has investigated the inflammatory pathologic lesions of the cerebral ventricular walls. He has therefore studied the acute nonspecific ependymitis accompanying severe meningitis and meningo-encephalitis. He also reviews and contributes to the study of acute and chronic tuberculous involvement. In the pathogenesis of ependymal tuberculosis

he distinguishes two fundamental pathways of infection of the ependyma: (1) direct, by apposition or by graft of the infectious material on the ventricular surface and (2) the vascular and the perivascular pathway of diffusion of the virus along the blood vessel walls originating from the meninges or from circumscribed foci in the nerve tissue. He also describes the pathology of acute and subacute ependymitis due to actinomycosis, which he studied experimentally.

Redaelli thinks that a distinction is necessary between ependymitis and ependymopathia. Ependymitis occurs in acute or chronic forms, which manifest themselves through typical histologic inflammatory changes (nonspecific ependymitis, syphilitic ependymitis, tuberculous ependymitis, etc.). Cases of ependymopathia are not related to inflammatory changes but to dystrophic conditions, vascular sclerosis or mechanical or chemical chronic stimulations, or they may represent the end-result of previous ependymitis (ependymopathia of chronic internal hydrocephalus or of senility, the granular type, the reticular type, the variolar type, the hypertrophic type, etc.).

FERRARO, New York.

CUTANEOUS SENSORY THRESHOLDS IN NORMAL CONDITIONS AND DURING CORTICAL STIMULATION AND FATIGUE. H. GRIESBACH, J. f. Psychol. u. Neurol. **41**:329, 1931.

The skin in the region supplied by the trigeminus tract is one of the best areas for esthesiometric investigations. In all investigations of this type it is absolutely essential to know the normal threshold of sensibility, which ordinarily varies according to the site of the skin which is being tested as well as according to the age and sex of the patient. The size of the threshold depends on whether there is a predominance of stimulation or of fatigue. If the threshold is lowered by stimulation just as much as it is raised by fatigue, the normal threshold, characteristic of psychic and somatic rest, may appear to be the individual's sensory threshold. Psychic effort causes predominatingly activation of the left cerebral hemisphere, whereas physical effort activates predominatingly the right cerebral hemisphere. According to this, the stimulation and fatigue associated with any effort, be it psychic or somatic, is distributed in varying degrees to both hemispheres. So that, as stimulation or fatigue prevails in the left or in the right hemisphere, the threshold of the skin is affected on the opposite side on account of the decussation of the sensory nerves. In health, during mental and physical rest, the normal threshold of cutaneous sensibility is equal or approximately so on both sides of the body.

KESCHNER, New York.

VOMITING OF PREGNANCY. VESTIBULAR FUNCTION. H. FREY and E. HERRMANN, Wien. klin. Wchnschr. **43**:545 (May 1) 1930.

During the first stage of pregnancy, vomiting is noted in about 50 per cent of cases. Weak irritation of the inner ear causes a change in the position of the eyeballs and of the head. Stronger stimulants, such as rotation, swinging and rocking, lead to vomiting and a drop in blood pressure. For these symptoms, vestibule, nerve and central connections are necessary, for it is apparent that vestibular reflexes may be influenced by the central nervous system.

Vestibular caloric tests were made on ninety-one pregnant women, of whom forty-nine were in from the second to the fifth month and forty-two from the eighth to the ninth month. Control tests were also performed on thirty nonpregnant women. Of the forty-nine women in the early stages of pregnancy, 91 per cent showed a more extensive labyrinthine reaction, while of the forty-two in the advanced stage, 69 per cent showed extensive labyrinthine reactions. However, only 43 per cent of the thirty controls showed this reaction. The author concludes that in pregnant women there exists a more pronounced vestibular reaction than in nonpregnant women. This increased capability is more noted in the earlier months of pregnancy, and it is concluded that the central nervous system governing the vestibular apparatus shows an increased irritability.

HART, Greenwich, Conn.

TRANSVESTISM OR EONISM. C. B. HORTON and E. K. CLARKE, Am. J. Psychiat. **10**:1025 (May) 1931.

The impulse to dress like one of the opposite sex is known as transvestism. It is not in itself evidence of homosexuality, as the garments may be conceived of as a fetish in a heterosexual desire. Horton and Clarke present two cases. One was that of a "woman," aged 32, who had been arrested with her husband on a liquor charge. She came of a family suffering from some glandular dystrophy (two of her grandparents each weighed more than 500 pounds [250 Kg.]), and was in childhood a circus performer. She had married at the age of 24. Examination disclosed that the patient was definitely a male with testes, penis, hair on the chest, hair on the face that had to be shaved daily and pubic hair of masculine type. Her "husband" derived his sexual gratification in extramarital adventures, while the "wife" stayed home and cooked, mended clothes and conducted the household. The authors believe that this patient's parents originally dressed him as a girl in order to exploit his strength as a circus performer. The second case was that of a boy, who derived great pleasure from dressing as a girl, using cosmetics and being associated at work with female employees only. He was overtly heterosexual. Havelock Ellis' statement that eonism occurs chiefly among the educated, sensitive and refined is not supported by these cases.

DAVIDSON, Newark, N. J.

ENCEPHALITIS PERIAXIALIS DIFFUSA (SCHILDER'S DISEASE). L. COENEN and LEON MIR, Encéphale **26**:357 (May) 1931.

The detailed clinical and pathologic observations in a case of Schilder's disease are presented. A man, aged 40, came to the hospital with blindness of the left eye and paralysis of the right leg and left arm, with the left half of the body almost insensitive. A diagnosis was made of multiple encephalitic foci in the two hemispheres. Death occurred six weeks later, after almost complete loss of cortical function. Autopsy showed softening and destruction of the white substance of the two hemispheres, with the gray substance practically spared. The appearance was very remarkable. In the zones the least degenerated there were infiltration of the vessels and mucous degeneration of the oligodendroglia. In the more degenerated zones there existed a complete destruction of myelin, which was phagocytosed by the microglia with the formation of granular bodies. The axis cylinders were partially conserved. The astrocytes were augmented in number and volume and formed a thick trellis-like arrangement. The perivascular spaces were filled with granular bodies and some lymphocytes. The authors consider the lesions of the oligodendroglia to be a result of a disturbed lipoid metabolism.

ANDERSON, Los Angeles.

CEREBELLAR DISORDERS IN DEMENTIA PRAECOX. JEAN TITECA, J. de neurol. et de psychiat. **31**:158 (March) 1931.

The author presents a case with mental changes fairly characteristic of dementia praecox. In addition to the mental changes present, there was evidence of cerebellar disturbances. He likens the case to some previously reported and termed "dementia praecox of cerebellar form." Macroscopically, there is a diminution in the volume of the cerebellum, involving a part of the hemispheres. Microscopically, there is a diminution in the number of the Purkinje cells. The author states that in necropsies cerebellar atrophy is often found in cases in which no clinical symptoms are noted, and he explains this by presuming a compensatory function of the cerebrum. In the patient the author describes there was a history of traumatism, and he considers that traumatism, particularly of the occipital region, is frequently followed by cerebellar symptoms, although in this instance he thinks that such was not the case because there were no acute cerebellar symptoms following the accident.

WAGGONER, Ann Arbor, Mich.

MENTAL AND PHYSICAL DEVELOPMENT OF CHILDREN PREMATURELY BORN. GEORGE J. MOHR and PHYLLIS BARTELME, Am. J. Dis. Child. **40**:1000 (Nov.) 1930.

After studying the mental and physical functioning of 713 premature children and comparing their performances with the achievements of 40 full-term siblings, Mohr and Bartelme conclude that the intellectual level of the premature child, as measured by the Gessell and Kuhlmann-Binet tests, is definitely higher than that of the full-term siblings. In studying 50 premature children who had brothers or sisters born at full-term, 33 showed the same relationship between mental and chronological age in both groups, while in 10 pairs the premature child was superior to the child born at full-term. In both groups, mean mental age exceeded mean chronological age, but this difference was 1.2 months in the group born at full-term and 2 months in the premature infants. Furthermore, 25 per cent of the premature children gave evidence of intracranial hemorrhage. Making allowance for the extent of the prematurity, there was no difference in the age of acquiring walking power, talking ability or bladder control.

DAVIDSON, Newark, N. J.

ON THE TREATMENT OF TABETIC OPTIC NERVE ATROPHY WITH SULPHUR. L. WINKLER, J. Nerv. & Ment. Dis. **73**:276 (March) 1931.

It has long been known that sulphur baths and mineral waters have had beneficial effects in inveterate syphilis, and in the tertiary form as well as in arsphenamine dermatitis the nutrition of the tissue improves. The author applies sulphur, in the form of intramuscular injections of from 0.1 to 0.2 cc. of a colloidal sulphur preparation, at the same time as bismuth in cases of tabetic atrophy. He obtained mildly elevated temperatures of from 101 to 103 F. He claims that sulphur acts particularly on ectodermic tissue, and that it does not act merely as a protein but interferes as a chemical atom directly with the metabolism of the cells. Ophthalmoscopic examination is stated to have shown changes of grayish discoloration of the disks into red, improved visual acuity, enlargement of the visual field and reappearance of color vision. The author dose not describe his cases nor does he state the number of cases tested or the number of controls.

HART, Greenwich, Conn.

PREANEMIC FORMS OF FUNICULAR MYELITIS. C. V. GOLMAN, Rev. psychiat., neurol. & reflexol. (Leningrad) **5**:57, 1930.

Hurst made an extremely important observation in cases of patients suffering from combined sclerosis; they did not have any free hydrochloric acid. With this consideration in view, the author reports three cases of paients who entered the hospital complaining of various subjective symptoms from which they had received no relief. These cases showed evidences of combined system disease, but without any evidence of blood dyscrasia. They also showed a glossitis and a lack of free hydrochloric acid. After the patients were given liver and were treated in all other respects as if they had pernicious anemia, marked improvement took place. The author believes that the combined sclerosis together with the glossitis and the achylia gastrica may be the only symptoms of a forthcoming primary anemia. In these cases liver becomes a specific form of treatment.

KASANIN, Boston.

TWO CASES OF LINDAU'S DISEASE. W. T. COLLIER, Brit. M. J. **2**:144 (July 25) 1931.

Two cases of capillary hemangioma (hemangioblastoma of Cushing and Bailey), one of the cerebellum, the other of the medulla, are described. Their association in each case with a small hypernephroma of the kidney entitles them to rank as cases of Lindau's disease, and their occurrence in two sisters illustrates the familial tendency of this disease. It is to be noted that in neither case was an angioma of the retina observed. In the first case this was not specifically sought; in the

second a macroscopic examination of the retina only was made, whereas an angioma may be of microscopic size. In neither case was the diagnosis made during life, and it is remarkable that in the first case, with very considerable involvement of the medulla, practically the only signs of disease were those due to increased intracranial pressure.

FERGUSON, Niagara Falls, N. Y.

THE SIMULTANEOUS REGISTRATION OF THE INTRA-OCULAR PRESSURE AND THE PRESSURE IN THE CEREBROSPINAL FLUID. E. MARX, Ann. d'ocul. **168**:125 (Feb.) 1931.

In continuing his researches, Marx has administered glandular extracts intravenously and noted the changes in intra-ocular and intracranial pressure. He found that the extract of muscle, thyroid extract, extract of placenta, ovary, thymus and liver and mamillary extracts and acetylcholine lowered the intra-ocular and intracranial pressure. Epinephrine and pituitary extract increased the pressure. The pressure in the two systems does not entirely parallel the changes in arterial pressure. Increasing the amount of injected material produced an increase in the changes in the intra-ocular and intracranial pressure, but the augmentation was not proportional to the quantity of material injected.

BERENS, New York.

ROLLER'S NUCLEUS. T. NAKAMURA, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **32**:61 (Oct.) 1930.

From his investigation of the comparative anatomy of Roller's nucleus Nakamura concludes that, like the nucleus praepositus hypoglossi, this structure belongs to a group of nuclei closely related to the triangularis. He looks on Roller's nucleus as a relay station for vestibular or triangularis stimuli. The position of this nucleus within the nucleus hypoglossi would seem to have some relation to the assimilation of food and to metabolism. The nucleus as such, however, is an independent structure and has distinct fiber connections in three directions: (1) to the dorsal longitudinal bundle of Schütz, (2) to the homolateral radiary fibers and (3) to the contralateral radiary fibers.

KESCHNER, New York.

LAZARINE LEPROSY. V. PARDO-CASTELLO and G. M. CABALLERO, Arch. Dermat. & Syph. **23**:1 (Jan.) 1931.

In lazarine lepropsy, as in other forms of Hansen's disease, sensibility is affected, and large pieces of ulcerating skin may be removed without causing pain. Lazarine leprosy is characterized by bullous formations, scars and mutilating ulcers. The lepromas and dystrophic manifestations of leprosy are absent. The onset is usually acute, beginning with an erythematous patch which develops into a blister, then breaks down, scars and ulcerates. The specific bacilli are found in the fluid from the blebs. Most patients recover from their acute attacks. Treatment is symptomatic. The ulcers should be packed and irrigated.

DAVIDSON, Newark, N. J.

TREATMENT OF MENINGOCOCCUS MENINGITIS BY CISTERNA PUNCTURE. THEODORE GOLDMAN and ALBERT G. BOWER, Am. J. M. Sc. **181**:414 (March) 1931.

The relative merits of lumbar puncture (forty-eight cases) and cisternal puncture (fifty cases) in meningococcus meningitis are compared. In the latter an average of two less punctures and 30 cc. less of antimeningococcus serum was received by each patient. The mortality rate for the cisternal route was 27 per cent less than that for the lumbar method. The authors used the needle of a gage, determined for the patient under treatment, that facilitated the outflow of the purulent fluid and the injection of the serum.

MICHAELS, Detroit.

Society Transactions

FIRST INTERNATIONAL NEUROLOGICAL CONGRESS

The American Neurological Association has every reason to be satisfied with the results, both scientific and social, of the International Neurological Congress.

The preparations for the congress, held at Berne, Switzerland, from Aug. 31 to Sept. 4, 1931, entailed a considerable amount of work on the American Committee of Organization, the president and, especially, the most efficient secretary, Dr. H. A. Riley, of New York. Acknowledgment must be made of the splendid cooperation given the American committee by the various national groups and, above all, by the Swiss Committee of Organization and by Dr. Charles Dubois, Dr. R. F. von Fischer and Dr. Pierre Schnyder of Berne. The Swiss secretaries and Prof. Robert Bing of Bâle deserve great credit for the perfection of the local arrangements, and the two prominent Swiss medical publications, the *Schweizerische medizinische Wochenschrift* (1931, nos. 35 and 36) and the *Archives suisses de neurologie et de psychiatrie* (vol. 27, pt. 2), should be mentioned for the special numbers they dedicated to the International Neurological Congress. In the latter (p. 234), the local secretary, Dr. Charles Dubois, published an excellent summary, "À propos de la genèse du Congrès neurologique international, Berne, 1931," definitely establishing the fact that this was the first International Neurological Congress, pure and simple, thereby, giving additional importance to the congress of 1931.

Of the general arrangements of the congress, it need only be said that there was a slight departure from the plan generally followed in large congresses, in that the vice presidents were given definite tasks, and each one was in charge of a definite part of the program, and was appointed chairman of some session. The eight vice presidents were present during the entire congress, and each deserves special thanks for the conscientious performance of the duties assigned to him.

These vice presidents, together with the president and the two chief secretaries, constituted a program committee that selected the papers that were to be presented. Almost four hundred were submitted to the committee. Two hundred and sixty-nine were actually on the program and were read; a few were presented from a supplementary list of ninety-eight. The program committee was not in favor of the idea that every one who registered at an international congress thereby secured the right to present a paper. The wisdom of this course was made evident during the meeting, as was also the selection of definite speakers who were to discuss parts of the four special subjects that had been selected for discussion at the congress.

On Monday, August 31, at 9 in the morning, at the Casino in Berne, the Congress was opened by Dr. Motta, vice president of the Swiss Confederation, in the presence of about eight hundred active and affiliated members from forty-three countries. (It was a special privilege to recognize Prof. William H. Welch as one of the honorary members of the congress.)

After welcoming the congress in hearty fashion and referring kindly to the memory of Prof. Paul Dubois, the father of the local secretary, Dr. Motta, speaking in French, acknowledged in especially cordial terms the importance of the initiative that had been taken by the American Neurological Association in the preparation of this congress. In a few happy words he referred to the importance of neurology and to its relations to many special branches of science.

He was followed by Prof. L. Asher, Rector of the University of Berne, speaking in excellent English, who welcomed the neurologists to Berne in the name of the university. On behalf of the university, Professor Asher referred to the pleasure of having Professor Pavlov, the octogenerian, present and active, and presented honorary degrees to Dr. Harvey Cushing of Boston for the wonderful work he had done and alluded to the pride that the University of Berne took in Cushing's work and to the fact that he had been a pupil many years ago of Prof. Theodore Kocher, Berne's famous surgeon, and the one of whom Berne and Switzerland will always be especially proud.

An honorary degree was also conferred on Sir Charles S. Sherrington, to whom Professor Asher referred as philosopher and man of science, also expressing great admiration for the work he had done, and alluding to his work under Kronecker.

Professor Asher explained that both Cushing and Sherrington had at one time been workers at the University of Berne, and only such could receive honorary degrees from the university.

Prof. C. Wegelin, dean of the medical faculty, speaking in German, greeted the members of the congress.

Prof. F. Naville, of Geneva, president of the Swiss Neurological Society, speaking in French, extended further greetings and compliments, and Professor Bing of Bâle, a truly remarkable polyglot, president of the Swiss Organization Committee, spoke in Italian, welcoming the congress and stressing the important relation of neurology to various branches of medicine.

All these introductory addresses, none of which exceeded ten minutes, were answered by the president of the congress, who laid especial stress on neurology as the fundamental specialty of medicine.

Immediately following the introductory addresses, the congress began its scientific work.

The subject of the first day's discussions was "Diagnostic and Therapeutic Procedures (Surgical and Otherwise) in Brain Tumors." This program had been arranged by Prof. Max Nonne of Hamburg, who acted as chairman of this meeting, with Prof. Edwin Bramwell of Edinburgh as second chairman.

The discussion was opened by Sir James Purves-Stewart of London, on the "Symptomatology of Brain Tumors." He was followed by M. Clovis Vincent of Paris, who spoke on the "Diagnosis of Tumors Obstructing the Aqueduct of Sylvius." Prof. Giuseppe Ayala of Rome presented a paper entitled the "Neurologic Symptomatology of Subtentorial Tumors," and he, in turn, was followed by Dr. Foster Kennedy of New York, with "Frontal and Temporosphenoidal Lobe Tumors."

All of the speakers adhered strictly to the time limit announced in the program, and in this way contributed to the orderly progress of the meetings.

Following the discussion of the clinical symptomalogy of brain tumors came a series of papers on "Histologic Diagnosis." Dr. Percival Bailey of Chicago, Dr. Wilder Penfield of Montreal, Dr. Roussy and Dr. Oberling of Paris and Professor Pfeifer of Halle had an opportunity to present the views for which each of them has been known to stand these many years.

"Roentgenologic Diagnosis" was presented in carefully prepared summaries by Prof. A. Schüler of Vienna, Prof. H. W. Stenvers of Utrecht and Dr. Ernest Sachs of St. Louis.

"Ventriculography and Encephalography" were discussed in excellent fashion by Dr. L. Guttmann and Prof. Otfrid Foerster of Breslau, Dr. Francis C. Grant of Philadelphia and M. Egas Moniz of Lisbon.

No doubt very few were able to follow all four official languages, but carefully prepared summaries of the various contributions were helpful, so that the majority of the audience were able and willing to give close attention to the various speakers.

The subject of the morning session was continued in the afternoon under the chairmanship of Prof. C. U. Ariëns Kappers of Amsterdam, with Dr. J. Ramsay Hunt of New York, as second chairman, Dr. H. A. Riley and Dr. Pierre Schnyder acting as secretaries.

The question of "Serodiagnosis of Brain Tumors" was discussed by Prof. V. Kafka of Hamburg and Dr. Frank Fremont-Smith of Boston.

Without any disparagement to any other of the contributors, it may be definitely stated that the chief interest of the afternoon session centered in the truly brilliant presentation of Dr. Harvey Cushing, who read a paper entitled "A Summary of Experiences with a Series of Two Thousand Histologically Verified Intracranial Tumors." He was followed by de Martel of Paris, who talked on "Postoperative Accidents in the Surgical Treatment of Cerebral Tumors"; by Dr. H. Olivecrona of Stockholm, on "Gliomas of the Cerebral Hemisphere," and by Dr. Puusepp of Tartu, on the "Operative Treatment of Gliomas." Unfortunately, Dr. Charles H. Frazier of Philadelphia, who had announced a paper on "The Pathology, Diagnosis and Treatment of Intrasellar Lesions," was not present.

"Radiotherapy" was discussed satisfactorily by Dr. Béclère of Paris and Dr. Cairns of London. "Radium Treatment of Hypophyseal Tumors" was presented by Prof. Oskar Hirsch of Vienna, who gave most encouraging statistics.

Dr. Tracy J. Putnam of Boston followed with a discussion on "Organotherapy in Brain Tumors." Then Prof. Max Nonne of Hamburg gave a brief and satisfactory summary of the conclusions that might be drawn from the day's discussion.

There was no doubt that the remarkable work that was being done in so many different countries in the attempt to handle the problem of brain tumors was rewarded by the brilliant results of recent surgical therapy.

Although the members of the congress may have been somewhat exhausted by the scientific discussions of the day, they were ready in very large numbers to attend the evening reception that was given to the members of the congress by the authorities of the canton and the city of Berne. This reception was held in a delightfully informal way at the "Schänzli" overlooking the city of Berne.

The authorities were surely not responsible for the fact that the weather was cold and rainy during the entire week, with the exception of the one day on which we had fortunately planned an excursion into the environs.

Tuesday morning's session, under the chairmanship of Sir Charles S. Sherrington of Oxford, with Prof. Henri Claude of Paris as second chairman, was devoted to the subject of "Muscle Tonus; Anatomy, Physiology and Pathology." The excellent arrangement of the program is evident from the mere mention of the names and the special subjects.

Dr. S. W. Ranson of Chicago opened the discussion with a paper entitled "Nuclei and Fiber Tracts Concerned in the Postural Reaction Elicited by Stimulation of the Mesencephalic Tegmentum." He was followed by Prof. Ken Kuré of Tokio, whose communication was entitled "Ueber die Bahnen des Muskeltonus und deren Endigungen."

Dr. T. Graham Brown of Cardiff read a paper entitled "Tonic Responses from the Midbrain"; Prof. Leon Asher of Berne spoke in German, in a very vivacious fashion, on "Der Einfluss des Sympathikus auf den Muskel und eine Analyse seines Mechanismus." Then followed, in rapid succession, papers by Prof. V. von Weizsäcker of Heidelberg, on "Elektrische Untersuchung des Tonus"; M. Frederic

Bremer of Brussels, on "Pharmacologie du Tonus Musculaire," and Dr. E. A. Spiegel of Vienna and Philadelphia, on "Zur Pharmakologie der Tonuszentren."

Dr. Pollock and Dr. Davis of Chicago were listened to attentively on the "Relation of Modifications of Muscle Tonus to the Interruption of Certain Anatomic Pathways," as was Professor Donaggio of Modena, speaking in Italian, on "Parkinsonismo encefalitico e lesioni cortico-nigriche."

Dr. Kinnier Wilson of London presented "Disorders of Tone at Different Physiologic Levels," and was followed by Dr. Ramsay Hunt of New York, on "The Static and Kinetic Systems and Their Relation to Muscle Tone." M. Cruchet of Bordeaux spoke on "Relations du tonus musculaire avec le syndrome parkinsonien," and M. Fedele Negro of Turin spoke on "Le tonus musculaire dans les syndromes extrapyramidaux." M. Andre Thevenard of Paris spoke on "Le phénomène de la poussée, réflexe d'attitude." Sir Charles S. Sherrington of London then gave a brillant summary of the morning's discussion, from which one was bound to infer that he wished he could find some substitute for the designation "tonus," and in that some others might be disposed to agree with him.

Beginning with Tuesday afternoon, the work of the congress was divided between a number of different sections, which were held in the various lecture rooms of the University of Berne. It would be impossible even to mention by title all of the noteworthy contributions that were delivered, but it was, after all, a matter of great importance that so many members of the congress could bring forward many of the special subjects in which they were interested.

Special reference may be made to the brilliant session on "Neurologic Surgery," which was held under the chairmanship of Prof. G. H. Monrad-Krohn of Oslo, during which Prof. A. von Eiselsberg of Vienna, speaking on the "Operability of Intramedullary Spinal Cord Tumors," and Prof. O. Foerster of Breslau, on the "Operative Procedure in Tumors of the Quadrigeminal Region," shared honors equally.

Dr. Adson's paper on "Sympathectomy: Physiologic and Clinical Effects" was notable, as were also the contributions of Dr. Weisenburg of Philadelphia on "A Study of Aphasia with an Attempt to Formulate New Tests," and Dr. Michael Osnato, on "Speech in Animals and Children and Its Integration with Intelligence."

At the same session, Dr. Wechsler presented his discussion on "Cortical Blindness with Preservation of Color Vision Following Carbon Monoxide Poisoning and the Question of Color Vision, Color Agnosia and Their Localization"; Prof. E. Niessl von Mayendorf spoke on "The Symptom of Cortical Blindness and Its Cerebral Mechanism."

In the clinicopathology section, the contributions of Dr. W. J. Adie of London, on "Premonitory Headaches in Leaking Aneurysm," and Dr. Macdonald Critchley London, on "Syndromes of the Superior Cerebellar Artery," may be especially mentioned.

All of the sessions were well attended, and there was one feature that was especially noticeable in contrast with other congresses, both in this country and abroad: The members were willing to give closest attention to an infinite number of papers.

On the evening of Tuesday, the members were rewarded by a delightfully arranged excursion to Worb, an hour's distance from Berne. Dinners were given at typical Swiss inns in a village little known to the average tourist.

All arrangements were perfect, and in spite of having to return to Berne about midnight, every one seemed pleased with the evening devoted to Swiss forms of entertainment.

In spite of the late hour at which the members returned, most of them were on hand the next morning for the excursion to Interlaken. Some of us were rather startled when the proposition was first made that the congress interrupt its work by a day devoted to an excursion. But the idea was an excellent one. It gave some the rest that they sorely needed. It helped to bring many into closer social contact, and even the elements favored the idea, for it was the only fine day of the entire week. The vast majority were satisfied in leaving Berne at 8 in the morning to take a special train from Interlaken to the Schynige Platte, and to get the superb view of the Bernese Alps; while a few more venturesome spirits left even earlier in the morning, took the mountain railway to the last stop on the Jungfrau and returned to Interlaken in time to join the others on the homeward sail on the Lake of Thun. The day in and near Interlaken was restful and enjoyable, and everyone was ready for work on the following morning.

The subject of Thursday morning was "Acute Nonsuppurative Infections of the Nervous System." The program had been arranged by Prof. Georges Guillain of Paris, who acted as chairman, and Professor Lugaro, of Florence, as second chairman.

The subject was introduced by Prof. Otto Marburg of Vienna, whose splendid and impressive presentation, entitled "Allgemeine Pathologie der nichteitrigen Entzündungen des Zentralnervensystems," deserves special mention. He was followed by Marinesco and Draganesco of Bucharest. Then Dr. J. Godwin Greenfield of London spoke on "Acute Nonsuppurative Infections of the Nervous System." Prof. Auguste Wimmer of Copenhagen spoke in French on "Les infections äigues, non-suppuratives du système nerveux." Prof. H. Pette of Hamburg spoke on "Eine vergleichende Betrachtung der akuten infektiösen Erkrankungen vornehmlich der grauen Substanz des Nervensystems (Poliomyelitis, epidemische Encephalitis, Lyssa, Borna'sche Krankheit)." André-Thomas of Paris spoke on "Le zona," and he was followed by van Bogaert of Antwerp, on "Situation des encéphalomyélites disséminées äigues," and by Buscaino of Catania, on "Sindromi encefalitiche e sindromi isteriche."

It seemed natural to hear Professor von Economo speak (in German) on "Infectious Nonsuppurative Forms of Encephalitis," and Professor Lewy of Berlin spoke on "Die Bedeutung der Einschlusskörperchen bei den sogenannten Virus-Krankheiten." Professor Cornil of Marseilles discussed "Sur le mécanisme et les conséquences de la lyse myélinique dans certaines infections à virus neurotrope." Professor Brouwer of Amsterdam spoke (in German) on "Myelitis After Smallpox," and Dr. Ferraro and Dr. Scheffer of New York, on "Encephalitis and Encephalopathia in Measles." Professor Kling of Stockholm presented some special points regarding the "Dissemination and Control of Epidemic Infantile Paralysis."

On the afternoon of this day, many important problems were discussed. Great attention was paid to Pavlov's address "Les neuroses expérimentalement réproductibles ches les animaux." The "Histology of Brain Tumors" was well discussed by Dr. Globus, and Dr. Strauss and Prof. E. Foerster of Greifswald.

In another section, the question of the "Relation of Splenohepatomegaly to Amaurotic Family Idiocy" was discussed by Professor Schaffer of Budapest, Dr. Epstein of Vienna, Frau-Dr. Spiegel-Adolf of Vienna and Philadelphia and Dr. B. Sachs.

The question of "Neuroses" also received ample discussion. Among those participating in this discussion were Professor Stransky of Vienna, Dr. Szondi of Budapest, Dr. Bychowski of Warsaw and Dr. Oberholzer of Zurich.

On Thursday evening, the official banquet was held at the Casino. Very happy speeches were made by delegates from many countries. More than five hundred members and affiliated members took part in this function.

On Friday morning, the last of the four subjects for special discussion was presented, "The Rôle of Trauma in the Production of Nervous Symptoms." The program was arranged by Professor Rossi of Pavia, who was chairman, with Prof. Otfrid Foerster as second chairman.

Professor Rossi, in a very impressive, almost dramatic, fashion, opened the discussion by his contribution on "The Fundamental Lines of Traumatology of the Central Nervous System." He was followed by Dr. Symonds of London, on "Diagnosis and Treatment of Cerebral States Following Head Injuries." Professor Veraguth of Zurich spoke on "Grundlinien des Referates über den Einfluss des Traumas bei der Genese einiger Nervenkrankheiten." Dr. Naville of Geneva gave a "Rapport sur les syndromes neurologiques consécutifs aux électrocutions industrielles." M. Jean Lhermitte of Paris gave an excellent review on "Commotion de la moelle épinière," and Professor von Sarbò of Budapest followed with "Syllabus zum Referat: Mikrostrukturelle traumatische Veränderungen des Nervensystems im Lichte der Kriegserfahrungen."

It was a matter of regret that Dr. Jelliffe, who had announced a paper on "The Traumatic Neuroses as Viewed from a Psychosociologic Standpoint," was not able to be present.

If there was any one inference to be drawn from all of these papers on trauma, it was that very minute structural changes often follow trauma when least expected or without giving any outward evidence of their occurrence.

The four subjects selected by the program committee for special discussion were no doubt well chosen. They were subjects that were evidently in everyone's mind, and no suggestions were heard as to the greater importance of others that might have been selected.

It was fortunate, however, that in the afternoon session of Friday special attention could be given to "Multiple Sclerosis," in which Prof. G. Steiner of Heidelberg, Dr. Richard M. Brickner of New York, Dr. Arthur Weil of Chicago and Dr. Ley of Brussels figured prominently.

The chairmen and secretaries of the special sessions held in the afternoon were carefully selected, so that a large number of the prominent members in attendance from many different countries could be given some special distinction.

At the conclusion of the discussion on trauma on Friday morning, an executive session was held at which the president of the congress presided. The special subject of the business meeting was to take action regarding the next congress.

Sir James Purves-Stewart and Dr. Kinnier Wilson presented an invitation from the Royal Society of Medicine to hold the next International Congress in London, in 1935, in connection with the celebration in London of the centenary of the birth of Hughlings Jackson.

This invitation was warmly endorsed by Prof. Georges Guillain of Paris and Professor Foerster of Breslau. It was accepted by acclâmation by all the members present, and the general feeling was expressed that the invitation of the Royal Society of Medicine was most welcome.

The question arose as to whether or not an International Neurological Association should be formed. After free discussion of this subject, there seemed to be some doubt as to whether or not there was a special need for the creation of such an association, and it was decided by general agreement that, after all, the chief function of such an association would be to make arrangements for the next

congress, and the suggestion was adopted, that since this is the case, it would be well to continue the present organization until 1933, when a meeting might be called, as had been done in 1929, two years preparatory to this congress, to consider arrangements for the congress, and to select the officers and appoint the delegations and committees that will have charge of the second congress.

In accordance with this, Dr. B. Sachs will continue to function as president, Dr. H. A. Riley as secretary-general and Dr. Charles Dubois as local secretary. The national groups will continue as constituted at present, but are at full liberty to make such changes in their respective organizations as they see fit. Notice of this must, however, be given to the secretary-general, Dr. H. A. Riley of New York, and to Dr. Charles Dubois, the local secretary in Berne.

An important meeting was scheduled for the last evening. Considerable dissatisfaction has been felt by many of the prominent neurologists of the world as to the general status of neurology and its relation to general medicine and to psychiatry.

A conference was called at the Bellevue-Palace Hotel in Berne, for the evening of Sept. 4, 1931, under the chairmanship of the president of the congress, Dr. B. Sachs.

The subject was presented by Professor Minkowski of Zurich, speaking in German, who has published a number of articles on this subject in various journals at different times. His chief contention is that in medical schools and in hospitals neurology does not get the recognition it deserves. He was followed by Dr. Weisenburg of Philadelphia, who gave an excellent account of conditions in the United States, where, fortunately, we have little cause for complaint. He was followed by Professor Lépine of Lyons, who gave a remarkable picture of the status of neurology in the schools and hospitals of France. Unfortunately, Dr. Kinnier Wilson, who was to speak for Great Britain, was not present, but the subject was dealt with in masterly fashion by Professor Nonne of Hamburg, one of the few professors of neurology in Germany.

Professor Haskóvec of Prague presented a paper entitled "La réforme des études médicales et la nécessité de créer des cliniques neurologiques spéciales," and Professor von Economo of Vienna presented the conditions as he knows them in Austria. The subject was brought to a close by Professor Rossi of Pavia and Professor Brouwer of Amsterdam.

In a most forcible address, Professor Foerster of Breslau pictured the conditions that need to be remedied, and as a result he was commissioned to draw up a set of resolutions. The sentiment of the discussion and the reforms that seemed to be desirable were embodied in the following resolution, which was unanimously adopted: "Neurology represents an entirely independent specialty in medicine. Unfortunately, this fact has not been sufficiently recognized in various countries. The First International Neurological Congress hopes that the Universities and Hospital Authorities of the various states will take active steps to further the progress of neurology."

The records of this informal evening discussion will appear in the small volume of proceedings that will be issued in the course of the next few months.

There is no doubt that the First International Neurological Congress with its many valuable discussions and its important contacts will be a milestone in the development of neurology and will help to establish the proper relations between neurology and other branches of medicine and surgery.

After this conference was over, the entire membership of the congress, including the affiliated members, were invited by the American Neurological Association to

a "Smoker," which brought together more than four hundred and fifty members in a happy, informal, farewell gathering. All agreed that the whole congress had been well worth while. It is certain that the majority of the members are looking forward to the second congress in 1935, when, under more propitious economic conditions, an even larger attendance may be expected.

The Editorial Committee of the congress decided that the individual contributions should be published in extenso wherever the authors desired to have them published, and that the congress should avoid the expenditure of huge sums, which would be involved if three or four volumes of transactions were to be issued. In view of existing economic conditions, it was decided to publish a small official volume of "Proceedings," which will be issued at an early day at a relatively slight expense to the individual members. It was also the opinion of the Editorial Committee that the contributions to the International Neurological Congress would be absorbed at a much earlier day in neurologic literature if they were to be published independently and were not to await the issue of voluminous transactions.

B. SACHS.

NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY AND THE NEW YORK NEUROLOGICAL SOCIETY

Joint Meeting, May 12, 1931

MICHAEL OSNATO, M.D., *in the Chair*

POSTOPERATIVE RESULT OF A CHRONIC RIGHT-SIDED HEMATOMA WITH IPSOLATERAL PYRAMIDAL TRACT SIGNS. DR. IRA COHEN.

In a man, aged 30, headache developed a few days after a fall. Three weeks later, dimness of vision and weakness ensued. Six weeks after the trauma, he had choked disks; he fell backward on standing or walking. There were: a right central facial weakness, increased knee jerk on the right, diminished abdominal reflexes, and an equivocal right plantar response. The spinal fluid pressure was 440 mm. of water.

Ventricular studies showed only a few cubic centimeters of fluid from each side. An exploration was performed on the left side, and nothing was found. A week later, ventriculograms showed a shift to the left. Ten days later, an exploration of the right side revealed a chronic subdural hematoma, following the removal of which there was prompt recovery.

The interesting features of the case were not only the difficulty in making a diagnosis of the lesion, but its localization in view of the ipsolateral signs.

DISCUSSION

DR. H. A. RILEY: Did Dr. Cohen stimulate the ascending frontal convolution electrically.

DR. I. COHEN: No.

DR. ISRAEL STRAUSS: This case presents a problem in diagnosis. I am not referring to the hemiplegia on the side of the lesion, because one understands today rather well the cause of such a symptom. There was one feature of the case that I cannot explain; none of my staff have been able to explain it; perhaps some one present may have a suggestion. The symptom is that when the patient

sat up in bed he fell backward; and when he stood up and attempted to walk, he would go from side to side, and, unless prevented, would fall backward to the ground. This symptom is sometimes ascribed to cerebellar lesions, the vermis or elsewhere, and yet, in this case there was nothing affecting the cerebellum, unless it was indirect pressure. It is true that occasionally symptoms of this type are explained by a midbrain lesion, and yet in this man there was apparently no such lesion, unless, and this is the one possibility of which I am not certain, the pressure exerted on the brain stem in that region was sufficient to interfere with the pathways to and from the cerebellum.

FAMILY PERIODIC PARALYSIS. REPORT OF A CASE. DR. EDWIN G. ZABRISKIE and DR. ANGUS MACDONALD FRANTZ (by invitation).

The patient, a man, aged 23, had suffered from intermittent attacks of flaccid paralysis since the age of about 7. The onset of the attacks was nearly always at night, beginning with a numb feeling in the back of the neck, followed by weakness of the legs, then of the trunk, then of the arms, and finally of the muscles of the neck. In severe attacks there was virtually complete paralysis of all the muscle groups mentioned. There was no involvement of the cranial nerves. The paralysis was flaccid, with decrease or loss of the deep reflexes. The attacks lasted from two to twenty-four hours. There was considerable sweating at the beginning and end of an attack. A systolic murmur, with enlargement of the heart to the left, occurred in several of the more complete attacks. Electrocardiograms gave negative results. All laboratory studies gave negative results.

A partial attack, e. g., that of one forearm, could be induced by local cooling.

The patient's mother had suffered from the same disease, and had died during an attack of paralysis at the age of 23.

DISCUSSION

DR. EDWIN G. ZABRISKIE: This case is still in the process of study, and we are attempting to make a fairly intensive study of the neuromuscular apparatus. We are fortunate in our studies of this boy because we can produce a typical attack at will. We have already demonstrated this by subjecting the boy's right forearm to a cold bath. After twenty minutes there was a complete attack in the right arm below the elbow. This will give a chance to compare the paralyzed with the nonparalyzed muscles, and will also give an opportunity for more biopsy studies. One biopsy was performed during an interval between attacks, and the same slight changes were found that have been reported by Schmidt: a rather large vacuolization within the fibers, an enlargement of the Cohnheim fields, and a splitting of the muscle fibrils.

DR. M. NEUSTAEDTER: The patient whose case I reported in 1921 had three maternal uncles afflicted with the disease, one of whom died in an attack. Several other cases have been reported of patients dying during an attack. Schmidt claimed from material taken for biopsy during an attack that particles of glycogen are deposited in the muscle fibers. In my case there was a high sugar content of the blood, 166 mg. Having in mind the contention of Schmidt that in such cases the calcium content of the blood is low, I found in my case the high calcium content during the interval between attacks of 20 mg. per hundred cubic centimeters, while during the attack in the paralyzed state it went down to 4.3 mg., one-half the normal value.

DR. RICHARD M. BRICKNER: Has Dr. Zabriskie discovered that specific temperatures produce any definite effects?

DR. SAMUEL BROCK: The relation of sleep to the onset of some of the attacks is an interesting feature about this case, which brings up some important comparisons and relationships. Several years ago I described the case of a young man suffering from narcolepsy and cataplexy. At times, following a narcoleptic seizure, a condition would develop in my patient that was precisely similar to

family periodic paralysis. He would go through the same wiggles and maneuvers as this patient, although he always managed to recover his full strength in about ten or fifteen minutes.

In his excellent article on narcolepsy, Levin stated that Rosenthal described this phenomenon as "verzögertes psychomotorisches Erwachen" (delayed psychomotor awakening) and called the attacks "Wachanfälle" (waking attacks). Wenderowic drew attention to the resemblance of cataplectic powerlessness to that found in family periodic paralysis. One wonders whether this is a disease of muscular origin, as many authors have believed, or whether the presence of a similar condition associated with narcolepsy and cataplexy does not point to the brain stem as the place of origin of the muscular flaccidity. In cataplectic paralysis, Adie believes that there is a condition of tonelessness "which is the clinical opposity of decerebrate rigidity." May not family periodic paralysis be explained on the same basis?

DR. FOSTER KENNEDY: À propos of what Dr. Brock has said, it is interesting to remember that all of the deep reflexes are lost following cataplectic and narcoleptic conditions, which closely resemble those described in family periodic paralysis.

DR. E. G. ZABRISKIE: So far as we have found, the calcium content of the blood during the interval between attacks and that during an attack, did not vary. The only remarkable feature in this patient's blood was a fairly high cholesterol content which seemed rather constant for six or eight different examinations. Once it was as high as 280 mg., and it was never below 240 mg. What that means I do not know, and I have not been able to find any explanation for it.

In reply to Dr. Brickner, only one attack was produced in the right forearm, which was immersed in a bath at about 48 F. We tried to maintain that temperature for a period of about twenty minutes by adding ice. The skin became bright red and remained bright red for a while afterward, even after we had removed the arm from the bath. There was no sign of cyanosis, but the attack was complete. All electrical reactions of the forearm, all direct myotatic irritability and all tendon reflexes were abolished. The only power that remained was slight flexion of the finger-tips and a slight power to adduct the thumb.

As for Dr. Brock's suggestions, all these cases have been compared from time to time with cases of migraine, narcolepsy and cataplexy, but as yet no definite link has been demonstrated.

EFFECTS OF TOTAL REMOVAL OF LEFT TEMPORAL LOBE IN A RIGHT-HANDED PERSON: LOCALIZATION OF AREAS OF BRAIN CONCERNED WITH SPEECH. DR. WALTER E. DANDY (by invitation).

In the first case reported, that of a man, aged 21, the entire left temporal lobe was removed. The amount of tissue, including a tumor, was 130 Gm. Four months after the operation, there was no defect of speech that could be attributed to the extirpation of cerebral tissue. At no time did the patient have auditory aphasia. There was a profound anomia immediately after the operation. This is still present in some degree, but is steadily disappearing. We have been taught that the center for auditory aphasia is in the posterior part of the first and second left temporal convolutions. From this case it is evident that auditory speech is not located in the left temporal lobe. The anomia was doubtless due to the trauma to that part of the brain mesial to the sylvian vessel, that is, in the parietal lobe. Otherwise there would have been no return of this speech function. Unquestionably there is, as a sequel to the operative trauma, a permanent defect of some degree in the part of the parietal lobe that is contiguous to the temporal lobe.

In the second case the entire left occipital lobe in which there was a tumor, was resected; the supramarginal and supra-angular gyri were included. The plane of the cerebral incision was vertical and slightly behind the postcentral gyrus. A month after the operative procedure, the patient shows an absolute visual aphasia. He is unable to read a letter; he can write perfectly from dictation, but cannot

read anything he has written. He has no auditory aphasia. He had a slight anomia, which has disappeared. He had an almost complete apraxia after the operation; this has also disappeared. The results in this case show that the center for auditory speech is entirely independent of that for visual speech; also that the area of the brain concerned in apraxia is immediately contiguous to the tissue that was removed, and doubtless occupies the postrolandic region.

Another case is cited of a patient who had a constant series of jacksonian convulsions beginning in the right side of the face. A small tumor was excised, together with a small zone of tissue surrounding the tumor. Unfortunately, that patient never recovered speech, so that he had a total motor aphasia, but no sensory aphasia. This case is mentioned to show that the motor speech center is in the region of Broca's area. The only reason to mention this case is that from time to time doubts have been cast on Broca's original localization of a motor speech center.

An extensive resection of the left frontal lobe is shown because it passes through the so-called Broca's area and does not cause motor aphasia. From several cases of pure motor aphasia it is my impression that the area concerned in motor speech is somewhat farther posterior than that shown in textbooks.

Slides were shown of the amount of the left hemisphere that may be removed without disturbance of speech.

Summarizing, the results of cerebral extirpations in human beings show that auditory speech is located in the parietal lobe, that visual speech is entirely distinct and separate anatomically from auditory speech, and that Broca's area occupies essentially the area described by Broca, except that it is possibly a little more posterior.

DISCUSSION

DR. FOSTER KENNEDY: It is not easy to know what part of this presentation to approach first. Dr. Dandy has demonstrated some facts that we already know, and has demonstrated them in an extremely competent manner.

I am in entire agreement with Dr. Dandy's position that the speech areas, that is to say, the functions of integration that have to be achieved in order to effect perfect speech, live in segregated areas. It is as though in certain areas of the brain there are cells that have a certain ability of function: a general function such as vision, out of which can be educated a distinct attribute, and that attribute is highly localized and can be destroyed. Similarly, a difficulty with the motor tract may not injure a man's ability in the least to lift a heavy bucket of water, but may entirely destroy his ability to play billiards.

For a considerable time I have thought, with Dr. Dandy, that Broca's area was farther back, and I think that it is just in front of the rolandic area. I think that the reason why Dr. Dandy's patient recovered was because the lesion was behind the rolandic area. There was a motor aphasia, and I think that it was really a kind of agnosia for speech; a loss of the proper feeling of the tongue, lips and teeth that resulted in an inability to form the proper sound.

I was much interested, and it was a new idea to me, that what we have always called temporosphenoidal aphasia was really parietal. One sees such agnosias, anomias and perseverations resulting from lesions of the temporosphenoidal lobe. I have been sure for a long time that the term auditory aphasia is not a good one. It is extremely rare for anyone to be so aphasic that he cannot understand heard speech. It is easy to wipe out a man's ability to know written speech. It takes a much larger lesion, or perhaps a more discrete lesion, to wipe out his heard speech. In severe temporosphenoidal lesions, the patient cannot write the symbols of speech easily, but I shall have to revise my former opinion as regards the place from which such a condition is produced.

Dr. Dandy mentioned a paper of mine in which I was able to give an explanation for the so-called crossed aphasias, that is, those occurring in people who, being right-handed and having a right hemiplegia, had no aphasia. I was able to show that many cases of the series collected occurred in persons of left-handed stock; that their right-handedness was really a sport of the stock, and that the brained-

ness was a stock brainedness and did not follow the handedness. I think that many of us have left-handed strains in our ancestry, and I should not be surprised to find that that left-handed strain in right-handed persons produced a condition in the brain by which the opposite side of the brain (from the usual speech area) was able to sustain the function of speech. Possibly some of the recovery of the boy whose case Dr. Dandy has reported may not be due to the parietal lobe undertaking functions regularly sustained by the temporosphenoidal lobe, but to the education of the opposite side which contains elements that are ordinarily dormant in function.

DR. ISRAEL STRAUSS: In my mind there is no question but that for clinical purposes we shall still have to adhere to the localizing symptoms that we are accustomed to attribute to certain localities of the brain. There is no doubt that we will still have to regard auditory aphasia as being in the temporosphenoidal lobe, or at least in close proximity to it, and that we will have to regard Broca's area as a center having an influence on motor speech. It was Marie who took exception to the localization of Broca's area in the left third frontal convolution, but we have all found lesions definitely placed in that part of the brain affecting motor speech. All of us have found lesions in the temporosphenoidal lobe when we have postulated them because of the presence of the so-called auditory aphasia. Dr. Dandy, however, may be correct in stating that the lower part of the parietal lobe is the seat of this disturbance in function. When a lesion exists in the temporosphenoidal lobe we would have to regard that symptom as due to pressure or edema. However, it must be borne in mind that occasionally temporosphenoidal lobe symptoms are found in cases of small abscesses in the temporal lobe, and it is hard to conceive that edema from a small abscess would cross the sylvian fissure and cause an edema in the lower part of the parietal lobe.

DR. MICHAEL OSNATO: Were serial sections made, and were studies made of the association pathways, particularly those of the inferior longitudinal fasciculus, which connects the occipital with the temporal lobes, and the long association pathway which connects the occipital pole of the brain with the island of Reil and, of course, the temporosphenoidal lobe, namely, the occipitofrontal fasciculus?

DR. JOSEPH E. J. KING: I have had no experience with complete resection of the frontal or the occipital lobe, but I have been rather impressed with the amount of destruction of the temporal lobe occurring in cases of abscess of the temporosphenoidal lobe in which no permanent aphasia remains. In some of these cases there were rather large abscesses, and one was large and not encapsulated. There is no question about the destruction of the brain substances in this region from abscess. It is not a displacing lesion but a replacing one, and it destroys that which it replaces, i. e., brain substance. I can conceive of an encapsulated tumor in this area that might displace or push some of the temporosphenoidal lobe out of position, but such is not the case in abscess of the brain.

I had one case in which an abscess of enormous size developed in the temporosphenoidal lobe following an operation, with the herniation of the abscess cavity, in which a complete hemianopia developed. When the hernia receded, the hemianopia cleared up. The patient has no permanent aphasia of any kind. This patient was operated on in 1922.

DR. GEORGE VAN NESS DEARBORN: It struck me at once that more should be said about the possible "education" of substitute parts of the brain. It seems to be taken as a matter of course, at least by implication, that no education of substitute regions of the brain can occur. However, I observe in reading the latest research literature that such education may take place to a very considerable extent.

DR. W. E. DANDY: There is another important point that I neglected to mention. We are taught that there is an auditory center for hearing in each temporal lobe. The total excision of the left temporal lobe shows that there is no auditory center in the left temporal lobe. Moreover, similar negative results for hearing have been repeatedly demonstrated from total extirpation of the

right temporal lobe. Unquestionably, there is a relationship between the tracts for hearing and the auditory center, but the connection must be in the parietal lobe. It has long been taught that other parts of the brain, even the opposite side of the brain, may assume the lost functions of speech, motor power, etc. I think that it was Broadbent, of England, who first proposed this theory. Victor Horsley strongly opposed such a view. I think positively that there can be no restoration of function by education of the opposite side of the brain. For example, after the total removal of a right hemisphere there will never be restoration of motor function in the left side of the body. Moreover, after resection of the left occipital lobe with hemianopia, there is no restoration of visual speech or of the hemianopia. It is true that many cases of motor aphasia and hemiplegia clear up in part or entirely. That is due to the fact that the actual destruction of these parts of the brain has been only partial, or, as in cases of edema, there may be no permanent loss of the areas controlling these functions.

EXTRADURAL VENTRAL CHONDROMAS: FAVORITE SITES; THE SPINAL CORD AND ROOT SYMPTOMS THEY PRODUCE AND SURGICAL TREATMENT. DR. CHARLES A. ELSBERG.

The ventral chondromas are slow growing, primary extradural tumors that are not rare. They were found in 14 per cent of our last series of one hundred spinal tumors and formed 36 per cent of the extradural growths. Their favorite sites are the cervical and the lumbar intervertebral cartilages, and they occur predominantly, but not exclusively, in the male sex.

The clinical history is frequently one of long periods of vague symptoms before definite evidence of a localized compression of the spinal cord can be recognized. Not rarely, however, the duration of the symptoms has been a remarkably brief one, from one to five months.

The clinical picture is that of compression of the cord from its anterior aspect, with definite motor disturbances, cutaneous sensory loss with relatively little involvement of tactile sensibility, preservation in most instances of vibratory and muscle-joint-tendon sense, and relatively infrequent involvement of the sphincters of the bladder and rectum. Subarachnoid block is much more infrequent, and the globulin and total protein values in the spinal fluid are considerably lower than those in other types of tumor compressing the spinal cord. The roentgenograms of the spine usually show no evidence of pathologic changes.

The combination of symptoms and signs with the results of manometric tests and examinations of the spinal fluid, together with the negative roentgenologic results, should make a correct diagnosis possible in many instances.

The growths are usually of small size and are derived from the posterior border of an intervertebral cartilage. They can be best exposed by a complete laminectomy, with incision of the dura, determination of the exact location of the growth and mobilization of part of the spinal cord by division of one or more slips of the dentate ligament. In the majority of instances, the removal is best accomplished by a transdural method, but in some instances in which the growth is in the lumbar region, an extradural approach to the growth is preferable after its exact site has been determined by intradural exploration.

The results after removal of the tumor were satisfactory in almost one half of the patients. There was improvement in about one-third, and no improvement in two patients who had advanced disturbances of the cord before the operation. With the earlier recognition of the growths, the results of surgical treatment should be as good as in operations for other types of spinal compression by benign intradural and extradural new growths.

DISCUSSION

DR. JOSEPH E. J. KING: I wish to express my thanks to Dr. Elsberg for bringing to our attention this group of tumors, local in type, which may have escaped notice in certain operations. A tumor of this type may explain why no

lesion is found at an operation at the expected site in some instances. It is indeed interesting to hear about these cases.

DR. LEO M. DAVIDOFF: Dr. Elsberg and Dr. Stookey, who have done the work on these tumors, have established a syndrome that was practically unknown a decade ago, so that now, at the Neurological Institute at least, when one sees a patient, of middle age or thereabouts, with a relatively long history of spinal cord symptoms referred to the anterior pathways of the spinal cord, with usually only partial or no block, and only a slight rise in the protein content, one feels fairly sure that one is dealing with the so-called chondroma, and this diagnosis is now conservatively made correctly in from 75 to 80 per cent of our cases.

DR. FOSTER KENNEDY: I greatly admire the skill with which Dr. Elsberg brought out the diagnostic points — the significance of the percentage of patients with subarachnoid block in such cases and the significance of the total protein content. Dr. Elsberg perhaps would like to say a word on the significance of the "maleness" of these conditions, why so many males are afflicted as compared with the infrequency of the condition in women. I wonder whether trauma might have anything to do with this condition.

Perhaps Dr. Elsberg will agree with me that many of these histories, revealing a process that is slow at the beginning and rapidly becomes malignant and fulminating, are rather like those in tuberculosis. In Pott's disease there is exactly the same thing, a background of discomfort and pain for years, often followed by a sudden onset in one week of complete paraplegia.

DR. S. P. GOODHART: Dr. Elsberg has again given us what may be really described as a brilliant contribution to the pathology of the spinal cord; the clinical application of this contribution is of no less importance. One of the three female patients was originally seen by me, and I had the opportunity of referring the case to Dr. Elsberg. This case belonged to the group that Dr. Elsberg has classified as the acute or rather rapidly developing form. The case was referred to me as one of brachial neuritis; the manifestations, however, were such as to warrant the immediate diagnosis of a lesion of the spinal cord, probably neoplastic. Dr. Elsberg immediately recognized the condition as one due probably to pressure from a chondroma. He removed the growth, and the patient made a complete recovery. I am sure that the operator's familiarity with this type of growth was an important factor in the recognition and removal of the neoplasm.

DR. SAMUEL BROCK: Does not the relative infrequency of a manometric block lead one to suspect intramedullary disease in addition? Is this same point of view not supported by the sudden onset or acute exacerbations in the later course of these cases? It seems strange that indolent, slow growing cartilaginous tissue should suddenly initiate such striking symptomatology. Is there not some pathologic condition within the cord to account for such a rapid onset of symptoms? May not this also explain the small amount of recovery attained in many of the cases?

DR. CHARLES DAVISON: Did Dr. Elsberg find in the cases of chondroma histologic structures of the nature of chordomas? Chordomas, which generally occur at the spheno-occipital and sacrococcygeal synchondroses, were produced experimentally in rabbits by injuries of the intervertebral disks. I mention this because of the remarks made regarding the relationship between trauma and chondroma.

DR. C. A. ELSBERG: The question asked by Dr. Kennedy, why these ecchondroses occur more often in man, and his suggestion that men are more subject to trauma, is very apropos. Postmortem investigations of the vertebral column, to which I referred, demonstrated a number of interesting facts, namely: that small cartilaginous outgrowths from the posterior portions of intervertebral disks occurred in 15.2 per cent of 368 cases examined, and furthermore, that such ecchondroses were found much more often in women. There must be some reason why in my cases the male sex predominated, and it is very probable, I think, that the suggestion made by Dr. Kennedy that trauma is more frequent in men is sufficient to explain the fact.

Regarding Dr. Kennedy's second question, whether tuberculosis had to be considered in these patients, I would say that in all of the cases tuberculosis of the bone was excluded on account of the negative roentgenologic results.

In answer to the questions raised by Dr. Brock, I would say: In our first cases there was uncertainty whether we were dealing with intramedullary disease or compression of the cord from its ventral aspect, but we soon learned that in expanding intramedullary disease complete subarachnoid block was frequent, as was a high protein content of the spinal fluid, while in the ventral chondromas an absence of block and slight increase in the protein content were frequent.

In answer to Dr. Brock's question why the symptoms so often come on acutely: For years, probably, there are periods when the small ecchondrosis suddenly comes into contact with the dura and the cord within it as a result of changes in mechanical conditions, more especially as regards the fluid buffer. When this occurs, the patient may have sudden symptoms, such as loss of control of the lower limbs, so that he falls down, momentary loss of power in an upper limb, etc. With these recurring traumas to the cord, changes within the cord substance occur. Finally, the relations between ecchondrosis and dura and cord become more intimate and permanent, and from that time on more acute symptoms occur. It is probable that recovery was incomplete in a number of patients owing to the fact that there were already irremediable changes within the substance of the cord when the operation was performed and the ecchondrosis removed.

It would require an extended discussion to consider the histologic differences between a chondroma and a chordoma. They are certainly closely allied. The original view of Virchow regarding the characteristic physaliferous structure in the chordoma has not been fully confirmed by later investigators. Schmorl and Andrae, in their publications, discussed the question whether the small ecchondroses were chordomatous. They called attention to the fact that, not so rarely, from the nucleus pulposus of the intervertebral cartilage, there are small outgrowths that penetrate the bodies of the vertebrae, which have the histologic features of rests of the notochord. In general, the chordomas are fairly rapidly growing tumors, when they once begin to increase in size, and most of them have a rather malignant course, different from the small, slowly growing cartilaginous excrescences from the posterior borders of the intervertebral disks.

CHICAGO NEUROLOGICAL SOCIETY

Annual Meeting, May 23, 1931, Elgin State Hospital

SIDNEY D. WILGUS, M.D., *President, Presiding*

A CASE OF PAGET'S DISEASE. DR. M. A. SCHILLER.

History.—E. W. B., a white woman, aged 60, was admitted to the Elgin State Hospital on Aug. 4, 1928. There was no history of nervous or mental disease in the family. Her early life and development had been normal. She was married at the age of 17, and had three daughters and two sons living and well; there had been one stillbirth. She did not use alcohol, tobacco or drugs. She made friends easily and was a leader in her community. She was interested in music and elocution, and played the piano well. Her husband said that she had "always had a temper."

About fifteen years before presentation, she noticed when she had difficulty in buying hats that her head had begun to enlarge and she had to dress her hair so as to make the enlargement less noticeable. At the same time, headaches developed which would last for several weeks at a time, and during which she obtained little relief from an ice cap and bromide. There were intervals lasting

two or three months when she would be free from headaches. The patient then became irritable and quarrelsome and was always "stirring up" trouble in the family. About five years prior to admission, convulsions developed, during which she would lose consciousness, fall, froth at the mouth and have jerking movements of the muscles. These would last for five minutes, and would be followed by a headache for four or five days. At no time did she bite her tongue or hurt herself. The convulsions occurred several months apart. The last one, the sixth, occurred five months prior to admission; she had had none now for over three years. At the same time the patient became more irritable. She had a disturbed spell during which she would not stop talking for several days and nights. She took a ride in a taxicab and did not have any money to pay for it. She said she was unbalanced, called the doctor in the middle of the night, and thought she was dying. She was taken to the Mary Thompson Hospital in 1925, where her husband was told that she had a mental condition; she was sent to a sanatorium, where she remained for six months. She improved somewhat and was taken home, where she did some housework, but she would exhaust herself because of talkativeness and overactivity. About three years prior to presentation delusions of grandeur developed. She thought she was very wealthy and the possessor of some very fine dogs. Her physician sent her to the Mary Thompson Hospital, where a roentgenogram of the skull revealed Paget's disease.

Physical Examination.—The skull was abnormally enlarged, measuring 32.5 cm. in circumference, with a prominence of the frontal bosses. The mandible was large, thickened and somewhat protruding. There was no deformity of any other part of the skeleton on inspection. The head and neck otherwise were normal. The heart and lungs were normal. The pulse rate was 80 and regular. The blood pressure was 160 systolic and 100 diastolic. The abdomen and extremities were normal. A neurologic examination was unsatisfactory owing to lack of cooperation, but no obvious abnormalities were described. There was some arteriosclerosis of the retinal vessels. Roentgen examination revealed Paget's disease (osteitis deformans) of the skull, pelvis, both femurs and the spine.

Mental examination revealed an irritable, boisterous and antagonistic woman. Speech was rambling and disconnected, and she had an oscillation of mood. In the hospital she had become demented and confused. She was untidy in habits, she drooled saliva, was practically vegetative, and had to be kept in bed.

Laboratory examinations gave negative results.

MULTIPLE SCLEROSIS WITH LHERMITTE'S SIGN. DR. CHARLES F. READ.

A man, aged 43, had been weak and unsteady on his feet since 1917. He had been unable to move his legs at times, but had never been really sick. He had had difficulty in walking, owing to weakness and incoordination of the lower extremities, which had been worse at intervals. He had been jaundiced several years prior to presentation, and he had had smallpox in 1911. He had had difficulty at times in starting the urinary stream. In 1917, when cutting wood, his hands became numb and he became unsteady and weak. He quit work for nine months, but insists that he was not sick. The left foot was more affected than the right. He then improved, but had had many recurrences followed by remissions.

Since the first attack, the hands and arms had not been especially affected. He had had no headaches or dizziness. He was a carpenter and followed his trade as much as possible. At the time of presentation he was digging ditches. He did not like to get off the ground.

Examination showed that the Romberg test was markedly positive. He reeled considerably when attempting to stand with the eyes closed, and said that this was his worst trouble. The cranial nerves showed nothing of interest, except some loss of vision in the left eye, the disk of which was very pale. The right eye was apparently normal. There was no nystagmus and no special speech difficulty. There was loss of power in the left lower extremity; the vibratory sensibility was poor in this extremity, while it was good in the right. There was no evident

Babinski sign, although it was a little doubtful on the right. The tendon reflexes were equal and brisk; the abdominal reflexes were not elicited. There was considerable incoordination of the upper extremities, but no actual intention tremor. Thus, after a duration of fourteen years', Charcot's triad was still absent. Spinal puncture had not been done.

When the patient bent his head he had a sensation like an electric shock, which he said "runs from his neck clean down to his feet." As he bent the head forward he experienced this sensation extending down the entire left side. This sign has been described by Wechsler and Lhermitte. The latter stated that it is an early sign, and should assist in making a diagnosis of multiple sclerosis. Others have said that they have found it early and again later, coming on after other signs have developed. The patient said that he noticed the sensation along with the appearance of some of the other symptoms of which he first complained.

This case, of the cervical type, is also interesting because the patient is still able to be about and at work after fourteen years, despite the fact that when he first noticed the disorder he "felt as if his arms and legs were disconnected, and did not know whether they were there or not."

A Case of Tabetic Form of Dementia Paralytica with Tremor and Contracture. Dr. I. Finkleman.

A white man, aged 43, was a clerk in the parcel post department at the post-office and was fairly regular in work. He was an agreeable sort of person of good habits, and was well liked. About eighteen years before presentation, he had a chancre for which he received local treatment. At about the same time he also contracted gonorrhea. He never had any skin lesions. He was married about fifteen years ago and was divorced from his wife seven years later. There were no children, but one miscarriage.

A year prior to presentation, the patient noticed a tremor in the left hand. He received a series of intramuscular injections of bismuth. In November, 1930, he had a convulsion, and was taken to the Wesley Hospital, where he remained only a short time before he was committed to Elgin.

The patient was undernourished and presented a marked flexion contracture of the phalanges of the left hand and an allorrhythmic tremor to the left upper extremity. He had shown no conduct disorder since admission to the hospital.

He had a convulsion, however, in which the muscles of the face, body and arms participated in clonic movements. He lost consciousness, but did not lose control of the sphincters and did not bite the tongue.

He was well oriented. There was some impairment in his memory for recent events, but he gave remote memory data correctly. Calculation was poor. General information and school knowledge conformed to the education he had received (he completed the seventh grade at the age of 14). Retention was poor. The patient had not expressed delusional ideas, and no hallucinatory experiences or paranoid trends were elicited.

The essential physical findings were: a blood pressure of 120 systolic and 76 diastolic; a systolic murmur, heard loudest at the apex and to a lesser degree over the aortic area. The pupils did not react to light, but reacted in accommodation; the left pupil was larger than the right; there was some perioral twitching, particularly when he attempted to show his teeth; there was some diminution of motion in the muscles involved in facial expression, and the eyes were more prominent than normal; there was a coarse fibrillary tremor on protrusion of the tongue.

There was a coarse tremor of the entire left upper extremity, which involved also the pectoral muscles; the rate was about 3 per second; the range varied from medium coarse to a wide movement. The tremor was flexor and extensor in type, but sometimes it was from side to side. It disappeared if the limb was supported, and increased if the forearm was supinated. It was more marked on voluntary movement. Abduction of the left arm above the horizontal was

not possible. There was a flexion contracture of the fingers of the left hand, the patient being unable to open the hand; the flexion was at the metacarpophalangeal joints and between the proximal and second phalanges; the distal phalanges of the ring and middle fingers were extended. The thumb was not involved in the contracture. The patient showed a disinclination to use the left upper extremity for any movement. The gait was not unusual. There was some swaying during the Romberg test. He was unable to perform the finger-to-nose test on the left side, the tremor becoming more marked and the hand oscillating wildly as the nose was approached. The patellar and achilles jerks were not elicited on either side. The biceps, triceps, radial and ulnar wrist jerks were present bilaterally. The abdominal and cremasteric reflexes were present bilaterally and were equal. No pathologic reflexes were elicited. The faradic current failed to cause extension of the flexed fingers of the left hand, although it caused extension in the corresponding fingers of the right hand. There was a generalized retardation of the perception of sensation. The response to painful stimulation was diminished, the diminution being more marked in the lower extremities. Touch sensation was not impaired. The patient failed to discriminate between moderate degrees of heat and cold in the lower extremities. Deep pressure sense was lost over the achilles tendons and over the testes. There was no loss in sense of position. Bone vibratory sense was present throughout. A mild slurring of syllables was elicited by test phrases. The left upper extremity, as compared with the right, showed an increase in tonus, and on passive motion the limb moved haltingly, lacking the smoothness of motion present in the right extremity. The muscles were uniformly somewhat diminished in size throughout the body.

The Wassermann and Kahn reactions of the blood were 1 +, and when repeated, negative. The cerebrospinal fluid showed 4+ Wassermann and Kahn reactions, 12 cells per centimeter, and a 4 + reaction to the Ross-Jones and Pandy tests; the Lange gold solution curve on two occasions was: 5555543331 and 5555543110.

Comment.—Although the patient did not present a mental picture of dementia paralytica, a diagnosis of the tabetic form of dementia paralytica was made on the basis of the occurrence of convulsions and the presence of the characteristic Lange colloidal gold curve.

The unusual feature in the case was the presence of tremor in the left upper extremity and contracture in the left hand. The characteristics of the tremor were not unlike those found in postencephalitis in rate and rhythm. The range was variable, and it disappeared when the extremity was supported. These features are occasionally observed in parkinsonian tremors. The tremor was not explained on a functional basis, because the patient presented too many signs and symptoms of involvement of the central nervous system. The explanation offered for the tremor was the presence of a syphilitic lesion of the corpus striatum. This caused the release of a lower physiologic mechanism. This explanation was made more tenable by the fact that the extremity involved in the tremor showed a somewhat greater amount of rigidity on passive movement than the other. The contracture present in the left upper extremity was more difficult to explain. It did not follow the pattern of a peripheral nerve lesion, and a lower motor neuron lesion involving the anterior horn cells was also excluded by the presence of tremor in the contractured extremity. There were no signs of involvement of the pyramidal tract. The contracture can be explained on a physiologic, rather than on an anatomic basis. When the patient made an attempt to extend the contractured fingers, a marked contraction of the flexors of the fingers was observed. They failed to relax, and thus did not obey Sherrington's law of reciprocal innervation. The same thing occurred on attempts to abduct and raise the left arm, when the pectoral muscles were observed to go into spasm.

Although the opinion was that too many obscure neuromuscular phenomena are explained by hypothetic lesions in the basal ganglia, the conclusion was reached, nevertheless, that this was a case of tabetic form of dementia paralytica, with a syphilitic lesion in the basal ganglia.

DISCUSSION

DR. CHARLES F. READ: This case has been very interesting to me; I have had some doubt as to whether it is not functional.

DR. R. P. MACKAY: In this patient, there is an obvious and fairly marked spasticity and contracture in the left arm. The biceps, triceps and supinator reflexes are exaggerated on the left side to such an extent that one must assume involvement of the pyramidal tract. The movements seen in the left arm and hand are not rhythmic, and are clearly asynergic. In fact, one sees contractions of single muscles without regard to the normal synergic grouping, and not obeying the laws of reciprocal innervation. Such contractions, in my opinion, cannot be explained as neurotic or functional. They seem to have something of a myoclonic character and suggest cortical irritation.

DR. I. FINKLEMAN: The movements disappear during sleep, but the hand retains the contracture. The rigidity is not such as is found in spastic paralysis, but is rather of the jerky, cog-wheel type found in postencephalitis.

COLLOIDAL STATES OF THE BLOOD (ILLUSTRATED WITH MOTION PICTURES).

DR. FRANK WRIGHT.

The methods used in ordinary clinical examinations of the blood are harsh and destructive. By this I mean that all evidences of the beautifully balanced colloidal system are destroyed, and such information as one obtains is secured from dead, fixed and stained smears, or evidence of metabolic substances, separated by very active chemical agents or induced colloidal states, such as are used in serologic reactions. The striking examples of gross intracellular motion of the leukocytes and the manifold activities of the serum, which represents some of the tendencies of the plasma, are lost entirely.

By taking advantage of the increased visibility furnished by the ultramicroscope and powerful illumination of the untreated serum and cells, one is permitted glimpses, at least, of activities in the living blood.

Clotting and Sedimentation.—It is not to be thought for a moment that what one sees represents the activities of the circulating blood. From the moment the needle punctures the vein, the blood begins to change. It clots more or less readily, and the manner in which it does so attracts the critical eye of the clinician. Some bloods clot quickly, with a small, firm, conical clot, which separates readily from the wall of the test tube. Often the white cells fall on the outside of the clot, to form a buffy coat. The serum is apt to be highly colored, often cloudy, sometimes opaque or red-tinged by hemolysis. This is the lytic or dehydrated type of blood.

There are bloods that clot slowly, forming a large, soft, bulky, gelatinous clot, with little serum, which tends to be light in color and usually clear. This is the hydrated type of blood. Abnormal bloods divide themselves into two groups, even to the eye.

If the blood is allowed to flow into sufficient sodium citrate solution in any standard tube, such as that of Friedlander, and the rate at which the corpuscles settle is noted, one finds that the blood that clotted quickly and gave the highly colored serum is usually the one that sediments most rapidly. Readings of eight, twelve or fifteen minutes are found, compared to an average normal of three hours or a prolonged (from five to thirty hours) rate sometimes noted in hydrated bloods.

Blood Chemistry.—One is led to believe that the various metabolites (dextrose, urea, etc.) occur in the blood partly in solution or suspension in the aqueous portion and partly attached to the protein. By attached I mean combined with or adsorbed by the protein. As practically all the methods commonly employed depend on the use of a protein-free filtrate, the quantities found represent those in solution only. The lytic or dehydrated type of blood shows, as a rule, an increase of one or several of the metabolites; while the fixed, stable or hydrated

blood has, on the other hand, quantities of the chemical constituents much below the average amounts found in solution.

The terms hydration and dehydration as applied to the proteins of the serum, refer to the water exchange, along with the other metabolites. When sugar, urea and other constituents of the protein molecule are separated and go into solution, a certain amount of water also leaves the protein. Again, when the chemical ingredients of the blood are reabsorbed by the protein, water accompanies them, and it also combines with the molecule.

Refractometric Index and Viscosity.—The refractometric index of the serum is as constant as is the temperature of the body, the average normal reading being 1.35. Dehydrated bloods range lower, a reading of 1.3455 carrying a grave omen as to continuation of life. Hydrated bloods range higher. In like manner, the viscosity of the serum is an aid in measuring the changes in it. The average serum viscosity is 1.75 times that of water, dehydration lowering and hydration increasing the viscosity, the usual range being from 1.5 to 2.

Ultramicroscopic Observations.—Helpful as these measurements are, they do not furnish an insight into the finer activities of the blood. If, however, one places a few drops of serum in the center of the cone of light of the dark-field or ultramicroscope, using a paraboloid or cardioid condenser, one can see many particles in both serum and leukocytes. In health, these particles are fairly small and uniform in size, deflect the light moderately and show very active brownian motion. There is shown in this film visual evidence of that elusive thing called "pep." Such serum contains so-called normal (that is, average) amounts of the usual metabolites, with a refractometric index close to 1.35 and viscosity about 1.75.

Dehydration.—When one looks at the serum of a patient exposed to the influence of acute infection, particularly of gram-positive type, or to chemical intoxication, the picture is quite different. The protein particles lose their activity and begin to divide into smaller, and eventually almost invisible, hazy particles. These are the submicronic and amicronic forms. While these particles are going into solution, certain portions remain insoluble, and these are characterized by their brightness and tendency to coalesce, forming large, white, often ringlike bodies, termed giants. Such serum contains an increased quantity of metabolites; the sedimentation rate is rapid and the refractometric index and viscosity are low. If the infection is acute or the intoxication overwhelming, the particles, after undergoing division and partial solution, tend to form a gelatinous mass. This is comparable to the change in state that occurs when gelatin sets or gels, the aqueous portion being enclosed by the protein. Technically, the dispersed protein becomes the surrounding medium, and the process is, quite naturally, called gelation.

Old age, hypertension and diabetes may be mentioned as examples of dehydration, with division of protein particles due to long-continued etiologic factors. The staphylococcic, streptococcic and pneumococcic infections furnish more acute pictures. Gelation is found in many postoperative pneumonias, massive collapse of the lung, toxemias of pregnancy and eclampsia.

Hydration.—Many long-continued infections, particularly those caused by gram-negative organisms, or chronic intoxications, of which alcoholism is a good example, furnish pictures of hydration. Here the large, bright, hydrated particles predominate. The motion is slower, partly because of their size, and giant or ringed forms are frequent. These particles tend to huddle, clump, agglutinate and precipitate. It is here that one sees more closely many of the phenomena familiar to the serologist and bacteriologist.

Considerable dehydration or lysis may occur without causing sufficient symptoms to attract a patient's attention. The frequency with which hypertension or glycosuria is stumbled on in the course of a routine examination may be mentioned. On the other hand, when hydration predominates, subjective symptoms are many and variable. This is true also when the condition is in the making and evidences of both processes are found. This is termed hydrodehydration or dehydrohydration, depending on which is the more marked. The term gelatohydration is also used,

but, as a rule, this suggests approaching gelation and should be reserved for this emergency.

Clinical interest in the changing colloidal picture grows as one watches the bloods of patients, especially those under treatment. Diabetes furnishes a good example, with high blood sugar, low viscosity and refractive index and a picture of small particles or amicronic shadows, usually with limited motion or even none.

The Action of Drugs.—At times the picture changes, because of the splitting off of fat as well as of sugar, and here the ultramicroscope reveals bright, lipoglobulin particles, and the refractive index comes up—is "out of line." When insulin is used there is a change in the protein colloids, as well as in the sugar, for insulin is a marked hydrator. When an excessive dose is administered, the deposition of the large, hydrated particles in the capillaries of the brain is the cause of insulin convulsions. It may be of interest to note that dextrose is not the only substance that can dehydrate them.

The majority of drugs in common use today are dehydrators. Digitalis, the halogens, cinchophen, drugs used for anesthesia, the barbitals and methenamine are good examples. When, however, the hydration is overcome and dehydration pushed to the point of gelatin, one gets so-called toxic action. The digitalis produces coupling of the heart beat, heart block or nausea; the iodides and bromides produce acne; cinchophen has a growing reputation for its unfavorable influence on the liver, varying from jaundice to acute yellow atrophy; the anesthetics are often the cause of postoperative nausea; postoperative pneumonia and massive collapse of the lung are also due to gelation; the barbitals produce dermatitis with great regularity, and methenamine often causes bladder tenesmus and hematuria.

It should be noted that digitalis works well when the patient's blood shows evidences of hydration (it is a dehydrator), but is toxic when the blood shows signs of dehydration. The same is true in regard to the barbital derivatives, the cinchophens and methenamine. Few new remedies are used by the students of McDonagh, but we do think that we are able to apply the familiar drugs more intelligently.

An interesting group of drugs has been developed by McDonagh—the so-called conductors—the administration of which causes the inactive protein particles to resume their brownian motion. Manganese butyrate often puts a stop to a long series of furuncles or carbuncles; the symmetrical ureas terminate many an infection promptly; and acetylsalicylic acid maintains its reputation as the greatest seller because of this property.

(A moving picture of the appearances of the blood serum and leukocytes, as seen under the ultramicroscope, made by Drs. Wright, Le Blanc and Zrunek, was exhibited.)

STUDIES IN CATATONIC STATES: EFFECT OF CARBON DIOXIDE AND OXYGEN. DR. LEAH L. LURIE and DR. F. LE BLANC.

The protein in the plasma is not in true solution, but is in the form of colloid particles. The colloid state of the protein particles is recognized by the presence of moving particles as seen by the dark field illumination or ultramicroscope. In health, these colloids are fairly small and uniform in size, deflect the light moderately and show very active brownian motion. This normal state of the colloids is what is called normal dispersion. In disease due to acute infection or to chemical intoxication, the colloids undergo profound changes, which can be studied and recognized under the dark field. The protein particles lose their activity and begin to divide into smaller almost invisible particles. Some of these particles go into true solution and free water and metabolities; some remain insoluble, and tend to coalesce, forming large, white, often ringlike bodies called giants. This state of the protein particles is called dehydration or lysis.

Long-continued infections or chronic intoxications give a different ultramicroscopic picture. The protein particles absorb water and metabolites. They increase

in size and diminish in number. The particles are a brilliant white; they move slowly, and when they agglutinate the clumps formed contain fewer particles than those that are formed in dehydration. Giants and ringed forms are frequent. These particles tend to precipitate individually or in masses. This state of the protein colloids is called hydration.

McDonagh of London was the first to correlate these ultramicroscopic observations with the physicochemical changes in the serum. In dehydration one finds the sedimentation rate — the rate at which the red blood corpuscles sink in the citrated plasma — shortened. In hydration the sedimentation rate is prolonged. The metabolites, as determined chemically, tend to increase in dehydration and diminish in hydration. The refractometric index of the serum, which is constant in health, is lowered in dehydration and raised in hydration, as is the viscosity of the serum.

The clinical interest of this colloidal picture of the blood is a guide to evaluate the effect of treatment.

With this changing colloidal picture of the blood in mind, Dr. LeBlanc and I undertook a study of the colloids in the blood of catatonic patients.

About five or six years ago, Lorenz and Loewenhart reported interesting observations on the awakening of stuporous patients after the inhalation of a mixture of carbon dioxide and oxygen. They began with 5 per cent carbon dioxide and rapidly increased the concentration to 20 per cent, giving the gases for one minute. The period of stimulation lasted about five minutes; the patients then relapsed into the former condition of catatonic stupor. Later, the concentration of the carbon dioxide was increased, and the length of the inhalation was extended to two minutes. The period of stimulation was thus increased to ten or fifteen minutes. With modifications of this method, periods of stimulation lasting up to twenty-five minutes were obtained, but the patients always relapsed into the previous condition immediately afterward; no permanent benefit was observed.

Karl Langenstrass modified this method still further. He gave his patients a preliminary course of pyrototherapy, raising the temperature on alternate days to 104 F., or more, by intravenous injections of Coley's fluid or typhoid vaccine, giving about fifteen such injections. Following this, the inhalation of carbon dioxide and oxygen was given, beginning with 5 per cent carbon dioxide and 95 per cent oxygen, and gradually increasing the former to 25 per cent and decreasing the latter to 75 per cent. At this point the inhalation was continued for from twenty-five to thirty minutes. Very striking results were obtained by this method. Patients who had been in stupor for from ten months to ten years improved gradually under this treatment, and started to work in the institution; some even went home and went to work.

Langenstrass reported only six cases, in four of which the results appeared to be permanent. It would be interesting to know if these were the only patients treated by this method, or whether these six were the improved ones from a larger group treated.

We have adopted a different method of administering carbon dioxide and oxygen combinations, by subcutaneous injections instead of by inhalation. We injected the gases with the Bayeux instrument, made in France. The instrument delivers a definite number of cubic centimeters of gas per minute. Our object was to see what effect, if any, such therapy would have on the colloids of the blood serum. We selected seven cases of catatonia; all of the patients being in almost complete stupor. Four to five injections of gas were given at about five day intervals, and physicochemical and ultramicroscopic examination of the blood was done in all cases before the treatment was started; all showed a marked hydration.

The first injection was from 1,200 to 2,500 cc. of straight carbon dioxide. The male patients received the smallest amounts. In them the absorption of the gas was markedly slower. In every case, after this first treatment, the colloids of the blood were dispersed to some extent, as indicated by a lowering of the refractive index and viscosity in all cases and changes in the ultramicroscopic picture to one nearer normal.

For the second injection, we used a combination of 30 per cent carbon dioxide and 70 per cent oxygen. We injected from 2,000 to 3,500 cc., with the result that most of the bloods returned to hydration, although not quite so high as before the first treatment. We returned then in some of the patients to straight carbon dioxide, and injected doses as high as 5,000 cc.; in others we used the combined gases in doses as high as 10,000 cc. We obtained mixed results. For the fourth and fifth injections we used in all cases only 500 cc. of straight carbon dioxide, and in all cases we found the colloids relatively dehydrated (see table). Clinically, although we obtained only a slight improvement, it occurred in almost every case treated.

Our studies proved that: 1. Physicochemical and ultramicroscopic examinations of the blood afford a fine objective method whereby one can evaluate the effect of treatments. 2. The colloids in the blood of all catatonic patients we examined were in a state of hydration. 3. Carbon dioxide is a dehydrator. 4. Dehydration alone of the colloids in catatonia is not sufficient to bring forth complete remission. 5. Other underlying conditions must be studied in every case individually, and the patient treated accordingly.

Nevertheless, we made one more attempt to treat the whole group of catatonic patients with one general method. We turned attention this time to the intestinal detoxication. Lewis Bruce, in 1906, was the first to make a systematic attempt to ascribe a toxic origin to the psychoses. The toxins that act as exciting causes of a psychosis he divided into: (1) toxins of metabolic origin, (2) toxins of bacterial origin, and (3) toxins of drug origin. He included catatonia and hebephrenia in the group of psychoses with toxins of bacterial origin. The view is taken that the organisms that produce these toxic conditions are probably normal inhabitants of the human body and become virulent through failure of the defenses of the body against organismal toxins, and that the weakness of these defenses is probably as much a part of nervous heredity as an unstable brain.

According to Cotton, the psychosis should be considered as a symptom, and often a terminal symptom, of a long-continued chronic sepsis or marked infection, the accumulating toxemia of which acts directly on the brain cell. Ford Robertson made a search of bacterial infections in thirty-two cases of dementia praecox and came to the following conclusion:

"Every case of dementia praecox that I have investigated has been found to be suffering from severe bacterial infections, involving especially the intestinal tract. No one of these infections is special to this malady; they may be found in cases of acute insanity and manic depressive insanity and not infrequently among the general public.

"On the ground of the observations I have made it may be stated as an incontrovertible conclusion that the bacterial infections from which the subjects of dementia praecox suffer are quite incompatible with health. . . . In my judgment these chronic bacterial infections are the most important of several factors that determine the mental disorder. They are the direct cause of the morbid process in the brain that destroys its efficiency as a mechanism and leaves it incapable of many normal motor sensory and psychical reactions. In the victims of dementia praecox we have to recognize a special type of inherent defective resistance to the action of bacterial toxins." He reported encouraging results by therapeutic immunization.

We have tried here to detoxicate a group of catatonic patients by subcutaneous injections of a stock vaccine consisting of strains of hemolytic streptococci and pathogenic gram-negative bacteria. A second vaccine consisting of nonlactose fermenters was injected intramuscularly. Eleven injections were given in a period of six weeks. The stock vaccine was begun with 0.1 cc. at weekly intervals, the dose being increased by 0.1 cc. at each subsequent injection. The other vaccine was given at intervals, about three or four days later than the first, 1 cc. intramuscularly each time. In conjunction with the vaccine therapy, we gave heptylresorcinol in capsules; three of our patients did not cooperate in taking them. These patients were given instead a 40 per cent solution of sodium ricinoleate.

Effect of Treatment on the Colloids of the Blood in Catatonic Patients

Case	Sedimentation			Sugar			Refractive Index			Viscosity			Ultramicroscopic Picture		
	Before Treatment	After Carbon Dioxide	After Vaccine	Before Treatment	After Carbon Dioxide	After Vaccine	Before Treatment	After Carbon Dioxide	After Vaccine	Before Treatment	After Carbon Dioxide	After Vaccine	Before Treatment	After Carbon Dioxide	After Vaccine
M. B.	.....	2′ 9″	2′30″	70 mg.	112 mg.	83 mg.	1.3523	1.3503	1.3527	1.9 / 1	1.7 / 1	1.8 / 1	Hydration with precipitation	Evidence of dehydration	Evidence of hydration
H. D.	1′50″	1′24″	2′10″	125 mg.	158 mg.	126 mg.	1.3541	1.3503	1.3502	2.3 / 1	1.8 / 1	1.6 / 1	Hydration with precipitation	Evidence of dehydration	Evidence of dispersion
F. G.	.....	1′45″	2′12″	110 mg.	155 mg.	70 mg.	1.3511	1.3499	1.3491	2.2 / 1	1.7 / 1	1.5 / 1	Hydration, precipitation rings	Dehydration some dispersion	Evidence of dispersion, add CO_2
J. K.	.....	2′20″	2′21″	120 mg.	150 mg.	72 mg.	1.3509	1.3502	1.3512	1.9 / 1	1.7 / 1	1.65 / 1	Hydration	Evidence of dehydration	Evidence of hydration
W. R.	1′25″	1′24″	2′56″	150 mg.	145 mg.	84 mg.	1.3521	1.3507	1.3504	1.5 / 1	1.8 / 1	1.65 / 1	Hydration rings	Some dispersion rings	Evidence of dispersion
C. S.	30″	1′ 9″	1′35″	180 mg.	175 mg.	90 mg.	1.3520	1.3482	1.3492	2.2 / 1	1.6 / 1	1.6 / 1	Dehydration, secondary hydration	Dehydration	Some dispersion, still, hydration, part
J. S.	1′45″	45″	28″	134 mg.	102 mg.	75 mg.	1.3530	1.3490	1.3505	2.2 / 1	1.8 / 1	1.6 / 1	Hydration with precipitation	Dehydration, some dispersion	Evidence of hydrodehydration

The blood was examined during these treatments by the same physicochemical and ultramicroscopic methods. The results, as will be seen in the table, were much less encouraging than those obtained by carbon dioxide therapy.

Clinically, only one patient showed a definite improvement and one a very slight improvement; the rest relapsed into the same condition as previous to the vaccine therapy. This detoxication therapy proved again that every case of catatonia must be studied and individual treatment given.

DISCUSSION

DR. KAMIL SCHULHOF: Elgin has the distinction of having as a resident the man who was the first to use McDonagh's methods in this country — Dr. LeBlanc, one of the authors of this paper. While the ordinary laboratory procedures serve for diagnostic purposes, McDonagh's methods tell us what to do and what to avoid. I was very skeptical two years ago. Having made and utilized about 500 examinations, partly on my own patients with internal diseases, partly on the varied material of a general hospital, I am convinced that J. E. R. McDonagh has contributed more to medicine and especially to therapeutics than any other living man. A physician may accept or reject parts of McDonagh's theory, but he will greatly enrich his therapy if he accepts McDonagh's results.

Neurologists probably know better than I how many futile attempts have been made to find some organic changes in catatonic patients. The serum picture presented today differs about as much from the normal as an erythrocyte count of 8,000,000 differs from the normal. It seems to me that it represents what might be called in more ordinary, and less accurate, terms an increase in the total protein content, but in at least four cases there was not the relative increase in serum globulins that one usually expects with such high refractive indexes. I believe that there is a possibility that the picture is partly due to anhydremia. It might be verified by determinations of the blood volume and blood counts. The treatment brought the refractive indexes toward normal, but the disproportionate lowering of the viscosity indicates a further shift toward the serum albumin and further possibilities of treatment.

I believe that Lurie and LeBlanc are the first to find grave objective changes in these subjects and to direct treatment consciously against these changes. There is hope that more can be done with something tangible to aim at.

DR. F. J. LEBLANC: This work was undertaken with the kind assistance of Dr. Read and Dr. Wilgus, and with the hard work of Dr. Lurie. We did not start it with the intention of obtaining remissions, but nevertheless some of the patients showed varied remissions lasting several weeks. The question was: What clinical results can we get if we use the carbon dioxide subcutaneously? Dr. Schulhof suggested that there was no danger in such administration, and we soon proved this to be the case. We worked with guinea-pigs, and the experiments showed that we could use fairly large doses, far larger than we had thought possible. I communicated with Dr. McDonagh, of London, who wrote that the dose of 1,000 cc., with which we started, was too large, but we had already dropped the dose to 500 cc., which seemed to give the best results.

Clinically, as Dr. Lurie said, the patients were all in the worst possible state, stuporous, untidy and so on, and we thought that if we secured any results at all it would be interesting. If one can lower the refractive index and viscosity of the serum in these cases, one is accomplishing something. We resumed treatment with carbon dioxide in some of the cases later, if the patients did not do well with the vaccine alone, and we feel satisfied that the carbon dioxide has a better effect than the vaccine. In one case, the patient, who was very stuporous, did better on vaccine than on carbon dioxide, but this was not the usual result.

DR. CHARLES F. READ: From the clinical aspect, I have been greatly interested in the entire research. It fits in with work being done at St. Elizabeth's which has been reported in connection with the work of Lorenz and Loewenhart at Madison, and also in connection with a recent report of the National Academy

of Natural Sciences, where there was considerable discussion of the colloidal states of the cells, which seems to fit in with our investigation here. I have also recently come across some similar work by the Russians. What it all means is not known as yet. Perhaps one is getting just a peek through a keyhole instead of a look through an open door. I have watched these patients with considerable interest. They are all catatonic, and as is known, they may vary markedly in behavior from time to time. One of the patients, however, when I first saw him, was lying crosswise in the bed, with his buttocks sticking out. That was his favorite position and nothing one could do would alter it. Now he has changed considerably for the better. One of the patients who had been mute for several months, except during a period when we were giving him sodium amytal, went on a regular talking spree after an injection of carbon dioxide. One of the women also showed considerable improvement. I do not know how much any of these changes mean, but they are interesting in connection with the blood pictures presented, and I think that the research is well worth while.

Book Reviews

INDIVIDUAL PSYCHOLOGY. By ERWIN WEXBERG. Translated by W. Berán Wolfe. Price, $4. Pp. 415. New York: Cosmopolitan Book Corporation, 1929.

The translator in his preface says that the growing importance of individual psychology has intensified the need for a definite textbook of its theory and technic. He believes that Wexberg in the present volume has given such a work. The rational approach to the problems of mental life that this method offers, its simplicity and its humanism must appeal to all those who would understand and influence human behavior. "Individual Psychology" is the first book to show how far Adler has gone beyond his first announcement of the theory of organ inferiority and its psychic compensation, and it is to be hoped that it will dispel many of the misconceptions concerning the work of Adler and his school. Wexberg has succeeded admirably in describing the constructive and practical elaborations of the fundamental themes of the Adlerian psychology, and has demonstrated that individual psychology means more than the "inferiority complex" and the "will to power."

The introduction gives a historical review. Chapter I emphasizes the unity of the personality. Individual psychology, in contrast to psychoanalysis, never attempts to interpret a single isolated occurrence; conduct and experience can be interpreted only in their contextual relation to the total personality. Any single slip of the tongue or mistake, in itself, may have many interpretations; it is uncharacteristic and indifferent so far as the personality is concerned. Its values and interpretations become clear when it is properly placed in the mosaic of a personal pattern; i. e., when it is seen with reference to the "immanent teleology" that constitutes the very essence of personality.

The author distinguishes three forms of teleologic activity in the psychophysical organism: 1. The biologic, which is to be found in the entire system of reflexes that seem to "serve" any biologic end. "It is as if through thousands of generations an unconscious life-plan were at work with the one purpose of preserving life and the species at any cost." As a subgroup in this category he regards all those expressions of community feeling and living, foremost among them speech and logical thinking, that function as if directed by such a plan. 2. The rational, which initiates the "conscious and planful actions of men and the higher animals." 3. The personal, which might be said to provide in a narrower sense the theme of individual psychology.

In discussing the evolution of the personality it is brought out that the normal, well integrated person has objectivity, logical thought, willingness to work, willingness to experience nature and art and finally willingness to assume responsibility for all actions, thoughts, ideas and sentiments. This sense of responsibility has nothing to do with any moral responsibility, determined by a mundane or divine judge. It is the recognition of the fact that everything one does or experiences, with all its premises and all its consequences, is one's own work. Life's problems are the only practical tests of a man. These problems may be divided essentially into three groups: the problem of work, the social task and the sexual problem.

On the whole, the book is well written, concise and helpful to the physician who wishes to treat neurotic patients, or to the teacher who wishes to understand children. It is unfortunate that the translation should, at times, presumably in the interest of simplification, be misleading. This is notably the case in the discussion on heredity where it is said: "Individual psychology has extended its researches to their limit, and as a result nothing is left for the investigator of

hereditary predispositions to find." This is an inaccurate translation and gives a false impression of omniscience that is most unfortunate. This section in the original consists of a painstaking analysis of the elements of the heredity-environment problem in the endeavor "to explore to the utmost limits the effective value of individual experience" and to make use of the possibilities thus suggested in dealing with heredity as with any other given problem or condition.

The chapters on "The Family Constellation as a Factor in Personality Development" and on "Sex and Character" are the most important. In each of these there is a straightforward, simple explanation of neurosis as an escape from discouragement. In each the freudian theories are emphatically contradicted. For example: "The family relationship begins with the relationship between mother and child, if the mother is living. In complete contrast to the theories of Freudian psychoanalysis this relationship holds for both sexes." The "Oedipus complex" may occasionally occur in the course of a child's development, but it is always a secondary matter arising from some specific constellation. The closer bond between a child and a parent of the opposite sex, such as that of a girl to her father, is one of these specific situations. The closest relation of the little girl in the beginning is to her mother. The mother's interest in her infant develops the germ of social feeling so far as it is adequate to awaken confidence in her as the child's first sample of mankind and to pave the way to a confident attitude toward an ever-increasing circle. The parasitic relationship of the child to his mother does not indicate a true social feeling. A child who refuses to be separated from his mother for a moment, because of his dependency, does not necessarily love his mother — he simply needs her.

The fact that this is a "man's world" is emphasized in relation to sex. In spite of recent progress in the emancipation of women, most people still really feel that man is superior and woman inferior. The influence of this prejudice is unavoidably felt in early childhood. When a child asks about the secrets of sexual life his questions are bound up with a vital interest in his own person. He or she wants to know the status of the male-female relation. The questioning is not — as the freudians would have one believe — the expression of infantile sexual tendencies.

Masturbation is discussed at length in a direct and helpful way. It is looked on as one of the normal manifestations of adolescence. It is harmless until scolding by elders loads it with feelings of guilt. Shattered self-esteem brings out the neurotic elements with depression, remorse, perplexity and penitence. The youth, thinking himself a sinner, withdraws from the outer world because his emotional conflicts require more and more of his time. Given a certain hereditary predisposition, masturbation may be an introduction to dementia praecox, but only along the line of withdrawal still earlier set out on. Psychologically, this is not difficult to understand, for dementia praecox represents the final and complete retreat from the battle-front of life. The stupefaction (dementia) which the patient at first believes is the consequence of masturbation becomes the presenting symptom as interest in the outer world is lost.

In cases with no hereditary predisposition, neurosis may perpetuate masturbation. The neurotic person cannot relinquish the recurring indications of his own weakness or deprive himself of his constantly arraigned sense of inadequacy. He prefers to evade the actual problems of life by occupying himself in a futile conflict within himself. When a child grows and his inner security becomes established, the mood of inner conflict becomes paler and paler. In the course of time moderate masturbation, accompanied by a minimum of inner reproach, gives way to normal sexual intercourse, and the way is opened to a life based on reality.

The attempt of freudians to explain masturbation as the activity of "autoerotic impulse components" is no more than a restatement of the facts in sexual terms of the psychoanalytic philosophy, and is in reality no explanation at all.

Homosexuality and perversion are also discussed in a common-sense way. All these perverts are deserters from the battle-front of love. They are neither degenerates nor cripples burdened with hereditary stigma; they are simply neurotic

persons who lack courage to love and live. Among women the attitude which Adler has called the "masculine protest" has become intensified through the modern restratification of social and economic relationships. Neither "bisexual predisposition" nor "homosexual instincts" need be presupposed to account for the assumption of a quasi-masculine style of life. Rather it is found to be bad training from earliest childhood, revolt against the female rôle, the outcome of unfortunate experience and discouragement as to her own personal chances that have led to the sexual vagaries on the part of women. While it is true that personal ugliness or the presence of secondary male characteristics may have served as the occasion for worry as to her sexual rôle, the fact that numberless women similarly marked have none the less developed a normal heterosexuality, and others quite without such stigma have lived homosexually, falls into line with the whole adlerian teaching. Antagonism to the female style of life developed because of a misdirected personal striving for significance. The extreme type of masculine protest occurs most frequently when a little girl is crowded from the normal line of development by a trick of nature—by external masculine characteristics, such as ugliness, facial hair, masculine body, a deep voice and the like.

A notorious psychiatrist has called the individual psychology of Adler "a psychology for morons," and has questioned Adler's intellectual capacity. One might argue, however, that there are many "morons" in the world who need psychologic help and a great many folks too simple to join one of the pseudo-intellectual psychoanalytic cults. Any one familiar with the work of the practitioners of individual psychology knows that a great deal of direct, simple help is quickly given to neurotic adults and "problem children." Similar charges have frequently been made by thinkers who have feared in its great simplicity some too comprehensive system of human relations. Only those who have some experience in the application of the adlerian principles can be aware of the subtleties of perception, insight and explanation that render those principles of use.

PHYSIQUE AND INTELLECT. By DONALD G. PATERSON. Price, $2.50. Pp. 304. New York: The Century Company, 1930.

This book is one of the "Century Psychology Series" of which Richard M. Elliott, Ph.D., is editor. It is the development of material presented by the author in lecture form as part of a symposium and later as one of the articles in "The Measurement of Man." Scientists and laymen alike have theorized on and studied possible relationships between physical traits and defects and mental attributes until the literature has become voluminous and in some cases contradictory and confusing. The author well states his incentive to produce such a work by saying: "Undergraduates and graduate students alike were puzzled by conflicting conclusions in the literature and were eager to get systematically to the root of the available evidence in order to clarify their own ideas. Their enthusiasm prompted me to undertake for them a critical synthesis of the available literature, one which would enable the student to orient himself without consulting a relatively large number of scattered references."

The complex nature of the problems touched on is shown by the varied fields of knowledge which have been drawn on in making a summary of present-day opinion, and the result shows that opinion is far from being crystallized in any of the fields. The necessity for accurate measurements and adequate statistical methods is stressed, as is also the inadvisability of attempting to classify mankind into types. The measurement of physical characteristics is given brief consideration, while measurement of intelligence is treated with greater detail and adequacy. The significance of individual differences in mental and physical traits, with especial reference to the influence of heredity and of environment in producing such differences, is given brief mention.

Chapter 2 deals with height and weight in relation to intellect. In this chapter the author shows the minimum amount of critical selection of material from the literature, but accepts and quotes with astonishing credulity the most extreme

claims of experimenters in the field of endocrinology. Under the subdivision entitled "Studies of Children," he becomes more critical in his quotation of statistical data and more capable in his analysis of the implications of these data. Parallel studies of adults are given brief mention. The possible influence of social status, with all that this connotes in the way of nutrition, hygiene, food, training and environmental and cultural influences, is dismissed with inadequate consideration. The slight correlation that is shown in terms of averages for the mass between intellect and height or weight almost completely vanishes when the individual is considered alone, and this makes it impossible to use height or weight as an index of intelligence in an individual case. The conclusion reached in this chapter is that the significance of physical size with reference to intelligence is far less than is commonly believed and claimed.

Chapter 3 deals with cranial measurements and intelligence. Numerous studies and classifications of the size and shape of the head are referred to and are presented in tabular form. The conclusion is reached that, from a phylogenetic point of view, increase in head size and cultural evolution have in general gone hand in hand, but that individual variation in head size is, however, a function of race, sex and family stock and not an index of intelligence. Neither is head shape found to be related to intellect in the individual case.

Chapter 4 purports to consider anatomic age and mental age. Quoting from Rotch, an important variation is said frequently to exist between the chronological age of a child, his physiologic age, his anatomic age and his functional cerebral age. The measurement of skeletal development by means of the x-rays and studies of the relationship between such skeletal (anatomic?) age and the mental age, which in the hands of earlier workers seemed a promising field for investigation, are shown to be uncorrelated or weakly correlated with intellect, scholastic ability, social potentiality or emotional life. Pubescence or sexual development and eruption of the teeth are considered and dismissed as unreliable indexes of physiologic and anatomic development, respectively, and all are relatively independent of mental development. "Various aspects of physical growth are shown to be far from unitary. Therefore, no one phase of physical status is an adequate index of physical maturity." "In conclusion and on the basis of available evidence, we may say that height, weight, size and shape of head, anatomical development, pubescence and dentition do not provide us with a physical basis of intellect."

Chapter 5 enters into a consideration of intelligence as a "most complex trait," and takes up the morphologic theories of the late Dr. Sante Naccarati as well as other complex and simple indexes of body build, only to discard any physical measurement or experimental combination that has been tried out as an indicator of the mental development of an individual man.

Chapter 6 shows again a regrettable tendency of the author to becloud the issue by the use of variable and nonsynonymous terms. The title of this chapter is "Physical Condition and Mental Efficiency." In this chapter the work on the influences of malnutrition, various forms of physical disease and physical defect (mainly with reference to adenoids, tonsils, dental impaction and caries, hookworm infestation and the vague and poorly defined "intestinal toxemia") is summarized. Glandular dysfunction is again treated in a very uncritical manner with but few references out of a great mass of literature and with all the bias of the original author. Under other physical conditions, about the only point considered is inoculation with typhoid vaccine. Epidemic encephalitis is given brief mention along with meningitis, poliomyelitis and birth injuries. The conclusion is reached that "with the exception of diseases and injuries involving the central nervous system itself, it would appear that we cannot explain . . . individual differences in intellect on the hypothesis that unfavorable physical condition or specific physical defects are operative as a major causal factor."

Under the heading "Physique and Temperament," chapter 7 devotes fifty-five pages to various aspects of the subject. Physiognomic traits are discussed in relation to temperament. Morphologic types and their relation to personality

traits are reviewed. Body build and physical defects are considered with especial reference to Adler's concept of organ inferiority. The Kretschmer theories relative to physical constitution and psychotic temperament are reviewed, and references are made to much of the recent literature bearing on this subject. The researches of Cannon, Crile and others on biochemical approaches to the personality problem are given consideration. A consideration of the psychologic and anthropometric measures of masculinity and a summary close this interesting chapter. The conclusion reached is that obscure relations between the functioning of the glands of internal secretion and physical traits and nonintellectual components of personality may exist, but that what is needed is less endocrinologic speculation in psychology and more psychologic experimentation in the field of endocrinology.

Chapter 8 is devoted to a general summary and conclusions. Here many of the conclusions of preceding chapters are restated and emphasized. The conservative attitude of the author is commendable, and he points out certain fallacies in the reasoning of various workers who appear to have approached the subject with some bias or to have done unscientific writing. The present status of the problem is given with suggestion as to continued research for its solution and a statement of the limitations of previous research.

The index of authors given at the end of the work omits but few who have produced worth-while contributions to the subject. The index of subjects could perhaps be improved by better subdivision and classification. The author is to be admired for attempting a definition of intelligence; he makes this more concise and understandable than most of the psychologic definitions of this faculty. Intelligence, he believes, is "abstract intellect, that is, the kind of intellect required for successful work in academic school subjects."

Throughout the book Dr. Paterson presents the attitude and technic of the statistical psychologist. One could perhaps be pardoned for wishing for a greater understanding of anatomic, physiologic and, in general, medical knowledge on his part and of a more critical selection of medical literature and of illustration. No gross errors appear, however, and the book must be accepted as supplying the need for which it was designed and as a concise and authoritative review of a voluminous literature produced on the subject during the past quarter of a century.

INDIVIDUAL PSYCHOLOGICAL TREATMENT. By ERWIN WEXBERG. Translated by ARNOLD EILOART. Price, 6 shillings. Pp. 160. London: The C. W. Daniel Company, 1929.

The introduction tells how in 1907 Adler published a monograph entitled "A Study of the Inferiority of Organs." This paper represented a successful attempt to place constitution-pathology on a new basis. With the help of a wealth of clinical material, Adler proved that weakness of certain organ systems creates a predisposition to disease. He indicated the possibility of the organism, physiologically and psychologically, compensating and overcompensating organ inferiorities. In the course of developments Adler turned his attention to psychology, and entered into close relations with Sigmund Freud. But the independence of Adler's ideas, which had their origin directly in the theory of organ inferiority and its compensation, led finally to the breaking of his connection with psychoanalysis. In 1912, Adler left the Vienna Psychoanalytic Union and joined with a number of collaborators and friends, for the further investigation of the way opened by him, the way of "comparative individual psychology." This school remains in agreement with the freudian doctrines so far as both lay essential emphasis on the subconscious or unconscious as containing the key to what had hitherto presented itself as utterly baffling in conscious emotional life. Both avail themselves of a special technic in the interpretation of dreams, of the "psychopathology of every day life" and of neurotic traits in general. But whereas Freud's interpretation is founded on his doctrine of the libido and is in a large measure causal in orientation, Adler's is fundamentally teleologic in emphasis. To him the question of prime import is: What will the individual, at what is he aiming, to what end does he make use of the given constitution or situation?

Today one has to do not only with a school of individual psychology within psychology, pedagogy and psychotherapy, but also with an individual psychologic movement, which has for its aim the scientific development of Adler's ideas, their propagation and their working out in the practice of almost all walks of life.

The theory of individual psychology is taken up in chapter II and is put forward much as in other books on this subject. Stress is laid on the point that to understand a person is to recognize the goals he has set himself, and on the two, at least partially opposed but at the same time mutually complementary poles, ego-feeling and community-feeling. It is emphasized that a number of important conditions of development for the child may be grouped together under the term "family-constellation." By this is meant the position of the child within the family, so far as this is determined by fate; e. g., the fact that one child grows up as the only one, another as the youngest, a third as the only girl among boys, a fourth without a father, and so on. These conditions of the child's development are ordained by fate; but of themselves they do not constitute a determination of his development. That depends on the question stated: How does he learn to interpret and to deal with these given conditions? And here is the keynote of adlerian emphasis on education. For more and more the effort of individual psychology is focused on education for the simple reason that herein lies the only promising possibility of a prophylaxis of nervous disease.

The books tries to be practical, so individual psychologic therapeutics takes up a large part of the text. The first and most important task of individual psychologic therapeutics is this: To understand the patient's malady as part of his personality, to recognize the directrix, or goal, of this personality and to refer all its mental expressions to this directrix. In the first interview one may gain a preliminary orientation, then the task of further treatments is, in general, to let the patient talk. If the narration ceases, one intervenes with questions the answers to which bring the necessary supplementation. In order to facilitate this task for the psychotherapeutist, the author gives a questionnaire which contains in systematic order the most important points on which one has to get information from the patient. The questionnaire is, of course, not to be applied literally.

The chapter on "The Sexual Anamnesis" is interesting because it points out so clearly the difference between the freudian and the adlerian point of view. This is especially well illustrated in the discussion of masturbation, which is looked on as nothing but the activity of a physiologically occurring pleasure mechanism. When Freud holds all pleasure mechanisms to be fundamentally the same, he is certainly right; only it is evidently improper to group them all together under the collective name of sexuality. To Wexberg it seems much clearer to say that some of the pleasure mechanisms that are at the child's disposal enter later into relation with sexuality; the linking of it with erotic fantasies gives it then specific sexual significance. The auto-erotic diversion of the sexual instinct enables the neurotic person to keep away from the other sex. It is an escape reaction and as such is a symptom of neuroses.

In great part the sexual behavior is only a special case of the behavior to people in general. It is easy to understand at once that persons who from youth have been anxiously concerned with the security of their personality have not learned the technic of association with their fellow men. Adjustment to the community succeeds only when it is really desired. The neurotic persons' dread of exchanging the family circle for the larger circle of human society is often obvious and can always be traced back to the attitude developed in his early childhood. Such dread constitutes not infrequently the first marked symptoms of nervous illness. There are few nervous symptoms which by way of "profit from disease" do not facilitate flight from one's fellows. It is easy to show that the community feeling forms an integrating constituent of the biologic character of mankind, and that in consequence every one who fails to adapt himself to the community must in some form or other bear the consequences. The neurotic person's view of life is characterized by three fundamental features: pessimism, as an immediate expression of his discouragement; fatalism, as the attempt of the poor-spirited

one to devolve on the fiction of Destiny the responsibility for his own lot which he dares not fashion for himself; hedonism, the misinterpretation of life as obligated to provide him only enjoyment with no obligation on his side. One often finds in neurotic persons a tendency to mysticism and superstition, an expression of the wish that there may be supernatural powers, because, for life as it is, they do not feel adequate and therefore would gladly comfort themselves with a hope in miracles.

The understanding of the personality of the neurotic person, including his neurotic symptoms, is the first and most extensive part of psychotherapy. Its second, pedagogic side may be characterized in one word, "encouragement." The attitude of the physician is important; as in the education of children, so in the education and treatment of adults, every emphasis on authority is set aside. A discouraged patient, who perhaps had to suffer from the authority of a strict father, will be all too readily inclined to seek in his relation to the physician a repetition of that which formed the essential characteristic of his nursery. One may, with the psychoanalyst, call this state of things "transference." This is a situation to be carefully avoided, for it is essential for the physician to keep himself on a basis of comradeship with the patient; if he allows himself to be looked up to and set on a pedestal there is immediately a return to the parent-child relationship of youth, and the pronouncements of the physician are toned with authority. It is just the demolition of the physician's authority and not its strengthening which is the concern of individual psychology. To be permanently beneficial to the patient, his relationship with the physician must be an example of how he should become socialized; perhaps this is the first real community relation that the patient has experienced. The psychotherapeutist should avoid giving the patient positive advice, much as the latter may lay himself out to obtain it, for the patient must learn to act courageously on his own responsibility. The treatment takes the form of a friendly talk, and a physical examination should always be thoroughly done before beginning treatment. The interviews should all take place in the physician's consulting room. Dreams are studied, for the general dream picture represents something like an allegory of that problem which is occupying the dreamer, but the daily events of life are equally important for discussion. These, and many other important points, are brought out in the chapter on "The Practical Conduct of Individual Psychologic Therapy, and the Pedagogic Side of It," the best chapter in the book, for it gives a useful picture of how the work is done. Such treatment may be applied to all functional neuroses and the functional psychoses if there be no amentia, dementia or delirium. Experience has shown that persons with manic-depressive psychoses, especially melancholia, can be treated beneficially.

For a small book this volume contains much well chosen and clearly expressed material; one wishing to gain an idea of what the "individual psychologic movement" is, and what it aims to become, can find it here in a few hours of reading.

A B C of Adler's Psychology. By Philippe Mariet. Pp. 116. New York: Greenberg, Publisher, Inc., 1929.

This little book is certainly not an "A B C" for beginners, but a closely argued brief upholding the adlerian point of view. The author is erudite in philosophy. It would have been better to have named the book, "Fundamental Conceptions of Individual Psychology." In the author's own words:

"This book attempts only to give the leading ideas of Individual Psychology, and a sketch of their origins. It is meant for the general reader who may be aware that he, like every one else, is a psychologist in practice, however unsystematic. Even the few proven principles here outlined would be, if applied to experience with sufficient alertness and elasticity of mind, of great help to the practical knowledge of human nature."

Chapter I discusses the basis of modern psychology, which seems to be the conception of the unconscious as vital memory — biologic memory. Freud took

the memories of success or failure in the sexual life as of the first importance. Jung tried to widen this view by seeking to reveal the superindividual or racial memories. Adler showed that the whole scheme of memory is different in every individual. Individuals do not form their unconscious memories all around the same central motive — not all around sexuality, for instance. In every individual is found an individual way of selecting its experiences from all possible experience. What is the principle of that selectivity? Adler has answered that it is, fundamentally, the organic consciousness of a need, of some specific inferiority which has to be compensated. It is as though every soul had consciousness of its whole physical reality, and was concentrated, with sleepless insistence, on achieving compensation for the defects in it.

The "Life Goal" is described in chapter II as the fictitious principle of individuality. It is the fantasy of what a person thinks he could be if things were not against him. It is the real end in view, or the focus of a man's practical conduct in life. It has usually very little relation to reality, never having been intended for realization in this world. Yet the influence of such an imagination on life is of paramount importance.

Adler acknowledges his indebtedness to Vaihinger's conception, which shows how all human knowledge, even that called the "exact sciences," is based on certain assumptions, which are thenceforth taken as if they were absolute truth. That which is called truth is in reality a "directive fiction." These directive fictions, meaningless in themselves, have the greatest importance in practice, because one works by them. In the psychology of the individual there is something of the same nature, a directive fiction which is not acknowledged just because it is implicit in everything the individual thinks and does. This determines the life goal, but they are so different in different individuals, that generalization is not safe; all, however, seem to have an imagination of superiority. Individual psychology aims to make a complete portrait of the individual and to divine the unconscious life-goal. This is important in neurosis when the life-goal threatens the conscious purpose.

Psychology in its relation to sociology is discussed in the next chapter, and here the "Adlerian School" is at its best. It is pointed out that psychology is making headway at last and coming into its own not only because it is biologically based, but because it is socially conceived. For the individual patient a new and better attitude can be obtained not by introspection with its further self-concentration, but by having the patient learn to give due weight to the attitude of others toward him. He can regain consciously the communal interest that he has unconsciously lost. Much that is helpful in treatment is condensed into philosophical form in this chapter.

The comparison of Freud's point of view with Adler's is done in a useful and moderate way. Some statements are too brief and emphatic to be accurate; for example, the statement that Adler has shown that "all psychopathology is of the nature of egoism." Perhaps a useful starting point for treating neuroses, but how about the mental activity in delirium, tumor of the brain with aphasia, etc.? Are not these also psychopathology?

This book cannot be abstracted, and it is difficult to review because it is so concise, so full of provocative implications. In places the style is somewhat exhilarated, but the logic is hard to controvert.

HEADACHE. By WILLIAM H. ROBEY, M.D. Price, $5. Pp. 247. EVERYDAY PRACTICE SERIES. Philadelphia: J. B. Lippincott Company, 1931.

The Everyday Practice Series is edited by Dr. Harlow Brooks, and as its title indicates it is designed for daily use by practitioners. The series already includes the subjects of posture, feeding, tropical medicine, burns and backache, reported by eminent clinicians. This newest subject, headache, has been prepared by Dr. Robey, a prominent Boston consultant and clinical professor of medicine in Harvard University. Dr. Robey employs a descriptive, historical and statistical

method in dealing with this material which results in a large amount of information that comprehensively includes but does not explicitly analyze or deal critically with a great many contributions on the subject of headache.

The volume is composed of an extensive collection of data on the common signs and symptoms of headache arranged in reference to the disease entities in which this condition is found. The main groups are constitutional, renal, infectious, hypertensive, cardiac, digestive and neurologic diseases. Present-day methods of treatment are adequately considered under each heading. This part of the book is especially useful.

Dr. Robey stresses the fact that headache is not a disease, but a symptom of disease that requires careful study. His opening words in chapter 1 indicate this, and in the following pages he outlines in order the important clinical steps. The first is a thorough medical history, and the second is a complete physical examination. These two matters are impressively important as one considers the vast number of headaches that accompany diseased conditions of organs and groups of organs.

The weakest part of the exposition is, of course, the section dealing with the pathology of headache. Since headache is a symptom of disease and not a disease itself, and since it can find its basis in a great number of bodily abnormalities, this is to be expected. The main causes are considered in chapter 4: increased intracranial pressure occurring, for example, in meningitis, the irritation and stretching of the dura such as occur in tumor of the brain, and headache produced by alterations in vasomotor tension. In explanation of the briefness of this chapter, Dr. Robey calls attention to the fact that actual changes within the cranial cavity have been the most difficult to observe and that at the present time theories on this subject are just now beginning to pass beyond the stage of conjecture. Chapter 2 is on the mechanism of headache and chapter 3 on anatomy; in these chapters many observations are quoted; especially interesting are those on the sympathetic innervation of the cerebral vessels, but no critical evaluation of data is given.

Some of the tabulations of the incidence of headache in hypertension and in diseases of the brain are quite valuable. They represent a careful study of a large number of cases at the Boston City and Peter Bent Brigham Hospitals and might well have been given more prominence than they receive in this book, which is primarily a survey of headache in all its clinical aspects. It is to be remembered, however, that this is a very broad field, and the fact that, as a whole, it is bewildering, is explained in recalling that the basic principles underlying these collected observations are only now beginning to be worked out by modern methods of neurology.

INTERNATIONALE TAGUNG FÜR ANGEWANDTE PSYCHOPATHOLOGIE UND PSYCHOLOGIE, Wien, 1930. Referate und Vorträge. Edited by H. HARTMANN, M. PAPPENHEIM and E. STRANSKY. Price, 17.60 marks. Pp. 241. Berlin: S. Karger, 1931.

Under the aegis of various European psychiatrists and psychologists, a society for psychopathology and applied psychology was founded about a decade ago. In June, 1920, the first International Congress was held in Vienna and many interesting papers were read.

Rudolf Allers discussed the importance of psychopathology for psychology, the theologist Karl Beth, its relation to religious psychology. The psychologist, T. Erismann, who is a follower of Spranger, described the position and reaction of the individual to society and the mass and the development of mass-reactions ("mass-psychoses"). Stransky pointed out the influence of present-day civilization on the individual, stressing especially the change from country to city life, unfortunate choice of occupation, etc. J. Suter reviewed the approach of applied psychology. W. Morgenthaler added to occupational therapy of patients their outlet in art productions, which ought to be encouraged and used as "creative" treatment,

as Jung had previously suggested. H. Prinzhorn offered a similar point of view with his presentation of the importance of Klages for psychopathology. Robert Wälder's paper gave an orientation of the metaphysical basis of the various modern psychologic schools. E. Hitschmann stressed the importance of psychoanalysis for pathographic studies. The historian Sigerist pointed out that it is not permissible to use one carefully analyzed case as a paradigm for a whole culture period. In analyzing a biography one has to try to understand the attitude of that person to that culture period, the attitude of the person who wrote the biography and one's own attitude. He also warned against believing in a continuous historical development of medicine and the comparison of ideas of various periods. The legal aspect of psychopathology was discussed by Eliasberg, Türkel and especially Hans W. Maier. The latter made concrete suggestions for changes in criminal laws. Luxenburger stressed the importance of heredity studies. Psychopathologic and general biologic heredity have in common that they deal with a reaction of the inherited disposition to environment, but in psychopathology also the reaction of the personality to the incipient or full-fledged inherited illness. What seems to be a clinical unit does not need to be a hereditary unit. This is especially important in the group of schizophrenias. The hereditary nucleus is a "complex of syndromes," especially represented by the hebephrenic and catatonic syndrome. Where one finds a mixture of endogenous and psychogenic elements one should use not the mendelian (statistical) method but a genealogic structure analysis (hysteria, psychasthenia).

Several short papers dealt with more specific psychologic and pathologic schools and problems.

THE PATHOLOGY OF INTERNAL DISEASES. By WILLIAM BOYD, M.D., M.R.C.P., ED. DIPL. PSYCH., F.R.S.C., Professor of Pathology in the Winnipeg General Hospital, Winnipeg, Canada. Price, $10. Pp. 837, with 298 engravings. Philadelphia: Lea & Febiger, 1931.

This book is of interest to neuropsychiatrists because it not only discusses the general pathology of the usual internal diseases but takes up extensively those in relation with the nervous system, to which it gives directly about 160 pages. In addition, there are chapters on diseases of the pituitary body, the thyroid gland, the suprarenal gland, the parathyroid glands and the thymus gland that are almost of equal interest.

The neurologic aspects can be recommended to the general practitioner and student without any reservation, but to the student in neuropathology and neuropathologists the work is entirely inadequate. For example, the discussion of the pituitary body covers 8 pages. In the part dealing with the nervous system, the pathology is up to date, but not as up to date as would be expected from a person who devoted his entire time to neuropathology. For example, in Huntington's chorea no reference is made to the work of Dunlap, which is by far the best that has been done on this subject.

On the other hand, the author has made this a readable book, for in addition to the pathology he also gives the clinical symptomatology; that is, he has coordinated the pathology with the clinical symptomatology, which is the only way that a book on pathology should be written.

THE MORBID PERSONALITY. By SANDOR LORAND, M.D. Psychoanalytical Studies in the Structure of Character and Personality. Price, $3. Pp. 181. New York: Alfred A. Knopf, 1931.

Among the numerous books from psychoanalytic sources, which may be considered as more or less a confession of personal faith and experience, the present book of Lorand constitutes a readable example with good records and clear examplification of principles.

The successive chapters cover childhood from infancy to puberty, difference in the early development of boys and girls, analysis of neurotic character types,

a case of sexual impotentia, indecision as an escape, the narcissistic type, a case of social inferiority, bisexuality, difficulties in female character formation, the wish fulfilment type, the revenge type, hysteric characters, psychosexual infantilism, crime in fantasy and dreams and the neurotic criminal, and a chapter on technic and therapy.

Evidently a capable pupil of Ferenczi, Lorand presents in direct and interesting form the essentials of the orthodox freudian formulations and developments of psychoanalytic treatments. There are occasional German usages of terms such as that of the word "instance" used in the sense of "Instanz." Otherwise, the fluency of the accounts appears unusually clear and concise.

DAS WUNDER IN DER HEILKUNDE. By ERWIN LIEK. Price, 3.60 marks. Pp. 206. Munich: J. F. Lehmanns, 1930.

Through the publisher of the *Münchener medizinische Wochenschrift,* Liek puts before the public his study of the miracle cures based on the "irrational aspect" of man and medical practice. It is indeed important that the medical student and the practitioner be reminded occasionally of the influence of certain inspired healers and the aspects of human nature that make possible some of the startling successes, like those of homeopathy, or some of the modern runs on a Coué or Geileis, an Austrian healer, etc. I might speak of the Abrams methods and so many other vogues. Liek's presentation is not as broadly illustrative of the human tendency to what Bleuler describes from so many angles in his "Autistic-Undisciplined Thinking in Medicine," but he makes the reader thoroughly aware of the rôle of the emotional factor in human reasoning and judgment and response to "treatment."